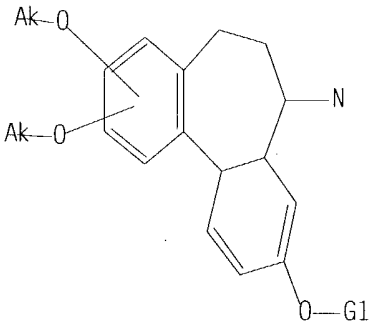
=> d his

(FILE 'HOME' ENTERED AT 14:38:56 ON 14 JUN 2004)

FILE 'REGISTRY' ENTERED AT 14:39:04 ON 14 JUN 2004
L1 STRUCTURE UPLOADED
L2 1 S L1
L3 39 S L1 FULL

FILE 'CAPLUS' ENTERED AT 14:40:16 ON 14 JUN 2004
L4 51 S L3

=> d que l4 stat
L1 STR



G1 Me,Et,n-Pr,i-Pr,n-Bu,i-Bu,s-Bu,t-Bu

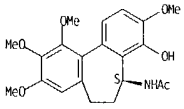
Structure attributes must be viewed using STN Express query preparation.
L3 39 SEA FILE=REGISTRY SSS FUL L1
L4 51 SEA FILE=CAPLUS ABB=ON PLU=ON L3

=> d 1-51 ibib iabs hitstr

L4 ANSWER 1 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:325968 CAPLUS
DOCUMENT NUMBER: 140:73942
TITLE: Occurrence of colchicine derivatives in plants of the genus Androcymbium
AUTHOR(S): Ellington, E.; Bastida, J.; Viladomat, F.; Simanek, V.; Codina, C.
CORPORATE SOURCE: Faculty of Pharmacy, Plant Biology and Edaphology, Department of Natural Products, University of Barcelona, Barcelona, Catalonia, 08028, Spain
SOURCE: Biochemical Systematics and Ecology (2003), 31(7), 715-722
CODEN: BSECBU; ISSN: 0305-1978
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Androcymbium gramineum plants were phytochem. investigated for alkaloids. Two major alkaloids, colchicine and demecolcine, were isolated from the whole plant, and 2-demethylcolchicine, 3-demethylcolchicine, N-formyl-N-deacetylcolchicine and colchifoline have also been identified by HPLC anal. This is the first report of demecolcine in A. gramineum, and of colchifoline in the genus Androcymbium. In addition, seeds of Androcymbium gramineum, Androcymbium hierrense, Androcymbium palaestinum, Androcymbium psammophilum, Androcymbium rechingerii, and Androcymbium wyssianum were also investigated for their alkaloid content for the first time. All were found to contain colchicine and colchicoside.

IT **126223-60-7**, Androbiphenyline
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(occurrence of colchicine derivs. in plants of the genus Androcymbium)
RN 126223-60-7 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-4-hydroxy-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



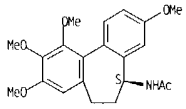
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 1 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L4 ANSWER 2 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:195822 CAPLUS
DOCUMENT NUMBER: 139:127393
TITLE: Novel B-ring modified allocolchicinoids of the NCME series: design, synthesis, antimicrotubule activity and cytotoxicity
AUTHOR(S): Bergemann, Silke; Brecht, Rene; Buttner, Frank; Guenard, Daniel; Gust, Ronald; Seitz, Gunther; Stubbs, Milton T.; Thoret, Sylviane
CORPORATE SOURCE: Pharmazeutisch-Chemisches Institut der Philipps-Universitaet, Marburg, D-35032, Germany
SOURCE: Bioorganic & Medicinal Chemistry (2003), 11(7), 1269-1281
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:127393
ABSTRACT:
Two new series of allocolchicinoids mimicking the structure of (-)-N-acetylcolchinol O-Me ether (2, NCME) were synthesized and evaluated for their abilities to inhibit tubulin assembly. Possible antitumor properties resulting thereof were evaluated in vitro on the human MCF-7 breast cancer cell line. The first series of NCME-derivs. was brought about by extending the seven membered B-ring to novel semisynthetic variations with a nitrogen containing eight-membered B-ring similar, for example, to the artificial, potent steganacin aza-analog 3. In the second series the seven-membered B-ring of NCME (2) was modified by annulation with a heterocyclic ring system. The racemic ketone 7a serving as key precursor involved in the syntheses of all the target NCME variants 9-13 and 15, 16 was easily transformed into the eight-membered B-ring lactams 9 and 10 via a Beckmann rearrangement of the corresponding E-oxime 8. The tetrazole annulated congener 11 was prepared via azidotrimethylsilane-mediated Schmidt rearrangement. Treatment of educt 7a with Bredereck's reagent led to the enamino ketone 14, which was easily converted into the pyrazole- or pyrimidine-annulated allocolchicinoids 15 and 16. Remarkably, all the allocolchicinoids 9-13 with an azocin-B-ring affected the tubulin/microtubule equilibrium only moderately. In contrast, the novel heterocycle annulated seven membered B-ring variants 15 and 16 proved to be highly potent tubulin-inhibitory, antimitotic agents. Interaction with tubulin occurred at concns. similar to those observed for colchicine (1) or the lead NCME (2). In all cases the antiproliferative effects correlated roughly with the inhibition of tubulin assembly.

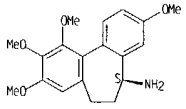
IT **65967-01-3** **84092-82-0**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis, antimicrotubule and antitumor activity of B-ring modified allocolchicinoids of the NCME series)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry. Rotation (-).



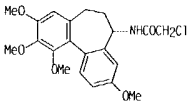
RN 84092-82-0 CAPLUS
CN 5H-Dibenzo[a,c]cyclohepten-5-amine, 6,7-dihydro-3,9,10,11-tetramethoxy-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:732415 CAPLUS
DOCUMENT NUMBER: 138:24856
TITLE: Antitumor agents. Part 215: Antitubulin effects of cytotoxic B-Ring modified allocolchicinoids
AUTHOR(S): Han, Shiqing; Hamel, Ernest; Bastow, Kenneth F.; McPhail, Andrew T.; Brossi, Arnold; Lee, Kuo-Hsiung
CORPORATE SOURCE: School of Pharmacy, Natural Products Laboratory, University of North Carolina at Chapel Hill, NC, 27599, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(20), 2851-2853
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:24856
GRAPHIC IMAGE:



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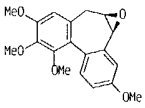


II

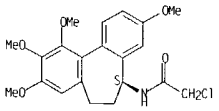
ABSTRACT:
N-Acetylcolchinol Me ether served as the starting material to prepare the chloroacetamide (I) and epoxide (II) analogs. Both I and II were potent inhibitors of tubulin polymerization in vitro. Compound I was also 4-fold more cytotoxic than colchicine against the 1A9 tumor cell line and showed a unique cross-resistance profile.

IT 478185-66-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of B-ring modified allocolchicinoids from N-acetylcolchinol Me ether and evaluation of their antitumor and tubulin polymerization effects)
RN 478185-66-9 CAPLUS
CN Acetamide, 2-chloro-N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

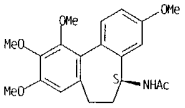
L4 ANSWER 3 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



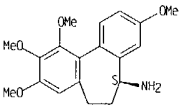
IT 65967-01-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of B-ring modified allocolchicinoids from N-acetylcolchinol Me ether and evaluation of their antitumor and tubulin polymerization effects)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 84092-82-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of B-ring modified allocolchicinoids from N-acetylcolchinol Me ether and evaluation of their antitumor and tubulin polymerization effects)
RN 84092-82-0 CAPLUS
CN 5H-Dibenzo[a,c]cyclohepten-5-amine, 6,7-dihydro-3,9,10,11-tetramethoxy-, (5S)- (9CI) (CA INDEX NAME)

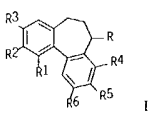
Absolute stereochemistry.



L4 ANSWER 4 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:90033 CAPLUS
DOCUMENT NUMBER: 136:151337
TITLE: Preparation of colchinol derivatives as angiogenesis inhibitors
INVENTOR(S): Arnould, Jean Claude
PATENT ASSIGNEE(S): Angiogene Pharmaceuticals Limited, UK
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008213	A1	20020131	WO 2001-GB2964	20010704
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1301498	A1	20030416	EP 2001-943701	20010704
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012225	A	20030506	BR 2001-12225	20010704
JP 2004504391	T2	20040212	JP 2002-514119	20010704
NO 2003000055	A	20030106	NO 2003-55	20030106
US 2003195173	A1	20031016	US 2003-332271	20030107
US 6720323	B2	20040413		

PRIORITY APPLN. INFO.: EP 2000-401976 A 20000707
EP 2000-401977 A 20000707
WO 2001-GB2964 W 20010704
OTHER SOURCE(S): MARPAT 136:151337
GRAPHIC IMAGE:



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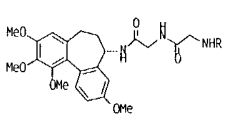


II

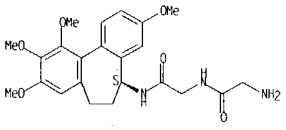
L4 ANSWER 4 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

ABSTRACT:
Colchinol derivs., such as I [R1-R3 = OH, phosphoryloxy, alkoxy, ester; R4-R6 = alkoxy; R = N(R7)-A-[CH(Ra)]a-B-[CH(Rb)]b-D; A = CO, ester, CONR8; R8 = H, alkyl, alkoxyalkyl, aminoalkyl, hydroxyalkyl; a = an integer from 1 to 4 inclusive; Ra, Rb = H, OH, amino; B = O, CO, N(R9)CO, CON(R9), N(R9)C(O)O, N(R9)CON(R10), N(R9)SO2, SO2N(R9), a direct single bond; R7, R9, R10 = H, alkyl, alkoxyalkyl, aminoalkyl, hydroxyalkyl; b = 0 or an integer from 1 to 4 inclusive; D = carboxy, sulfo, tetrazolyl, imidazolyl, phosphoryloxy, hydroxy, amino, N-(alkyl)amino, N,N-di(alkyl)amino, etc.], and pharmaceutically acceptable salt, solvate or pro-drug thereof, were prepared for their use as vascular damaging agents. Thus, reaction between colchinol I [R1-R3, R5 = OMe; R4, R6 = H; R = NH2] and 2[2-(tert-butoxycarbonylamino)acetylamino]acetic acid yielded II (R = BOC) which on treatment with TFA afforded colchinol derivative II (R = H). The prepared colchinol derivs. were tested against s.c. CaNT tumors.

IT **393784-98-0P 393784-99-1P 393785-01-8P**
393785-03-0P 393785-05-2P 393785-07-4P
393785-09-6P 393785-11-0P 393785-13-2P
393785-15-4P 393785-17-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of colchinol derivs. as angiogenesis inhibitors)

RN 393784-98-0 CAPLUS
CN Glycinamide, glycyl-N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

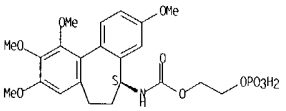
Absolute stereochemistry.



RN 393784-99-1 CAPLUS
CN Butanamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]-4-(phosphonooxy)-, disodium salt (9CI) (CA INDEX NAME)

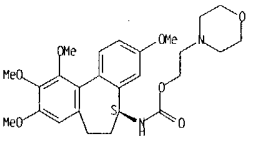
Absolute stereochemistry.

L4 ANSWER 4 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



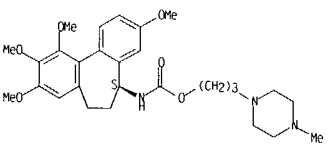
RN 393785-05-2 CAPLUS
CN Carbamic acid, [(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]-, 2-(4-morpholinyl)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



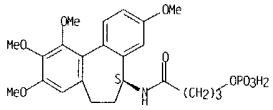
RN 393785-07-4 CAPLUS
CN Carbamic acid, [(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]-, 3-(4-methyl-1-piperazinyl)propyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



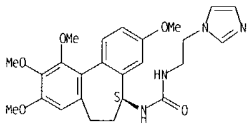
RN 393785-09-6 CAPLUS
CN Carbamic acid, [(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]-, 2-(4-acetyl-1-piperazinyl)ethyl ester

L4 ANSWER 4 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 393785-01-8 CAPLUS
CN Urea, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]-N'-[2-(1H-imidazol-1-yl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

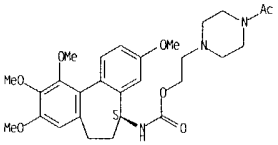


RN 393785-03-0 CAPLUS
CN Carbamic acid, [(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]-, 2-(phosphonooxy)ethyl ester, disodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

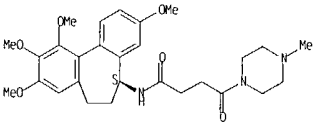
L4 ANSWER 4 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



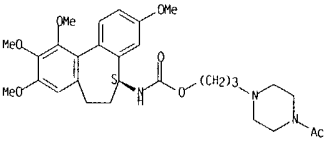
RN 393785-11-0 CAPLUS
CN 1-Piperazinebutanamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]-4-methyl-γ-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 393785-13-2 CAPLUS
CN Carbamic acid, [(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]-, 3-(4-acetyl-1-piperazinyl)propyl ester (9CI) (CA INDEX NAME)

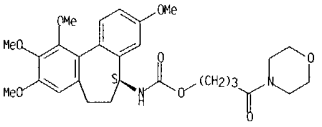
Absolute stereochemistry.



RN 393785-15-4 CAPLUS
CN Carbamic acid, [(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]-, 4-(4-morpholinyl)-4-oxobutyl ester (9CI) (CA INDEX NAME)

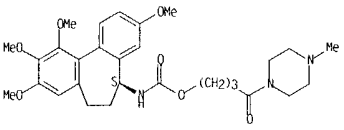
L4 ANSWER 4 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.



RN 393785-17-6 CAPLUS
CN Carbamic acid, [(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]-, 4-(4-methyl-1-piperazinyl)-4-oxobutyl ester (9CI) (CA INDEX NAME)

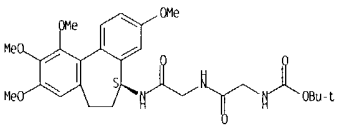
Absolute stereochemistry.



IT **393785-19-8P 393785-21-2P 393785-23-4P**
393785-27-8P 393785-29-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of colchinol derivs. as angiogenesis inhibitors)
RN 393785-19-8 CAPLUS
CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycyl-N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

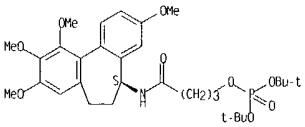
Absolute stereochemistry.

L4 ANSWER 4 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



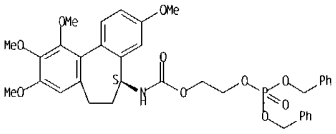
RN 393785-21-2 CAPLUS
CN Phosphoric acid, 4-[[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]amino]-4-oxobutyl bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 393785-23-4 CAPLUS
CN Carbamic acid, [(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]-, 2-[[bis(phenylmethoxy)phosphinyl]oxy]ethyl ester (9CI) (CA INDEX NAME)

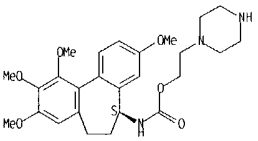
Absolute stereochemistry.



RN 393785-27-8 CAPLUS
CN Carbamic acid, [(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]-, 2-(1-piperazinyl)ethyl ester (9CI) (CA INDEX NAME)

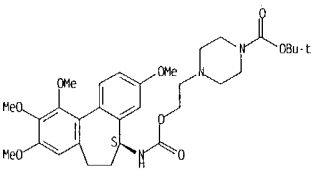
L4 ANSWER 4 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.



RN 393785-29-0 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[2-[[[[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]amino]carbonyl]oxy]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



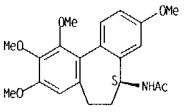
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:407821 CAPLUS
DOCUMENT NUMBER: 133:275861
TITLE: Self-organizing neural network for modeling 3D QSAR of colchicinoids
AUTHOR(S): Polanski, Jaroslaw
CORPORATE SOURCE: Department of Organic Chemistry, Institute of Chemistry, University of Silesia, Katowice, 40-006, Pol.
SOURCE: Acta Biochimica Polonica (2000), 47(1), 37-45
CODEN: ABPLAF; ISSN: 0001-527X
PUBLISHER: Polish Biochemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
A novel scheme for modeling 3D QSAR has been developed. A method involving multiple self-organizing neural network adjusted to be analyzed by the PLS (partial least squares) anal. was used to model 3D QSAR of the selected colchicinoids. The model obtained allows the identification of some structural determinants of the biol. activity of compds.

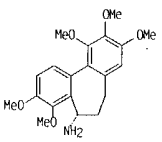
IT 65967-01-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(self-organizing neural network for modeling 3D QSAR of colchicinoids)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

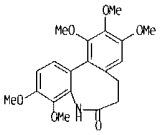


REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

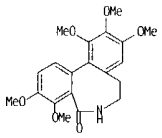
L4 ANSWER 6 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:157030 CAPLUS
DOCUMENT NUMBER: 132:322007
TITLE: Novel allocolchicinoids with an eight membered B-ring design, synthesis and inhibition of tubulin assembly
AUTHOR(S): Brecht, R.; Seitz, G.; Guenard, D.; Thoret, S.
CORPORATE SOURCE: Pharmazeutisch-Chemisches Institut der Philipps-Universitat, Marburg, D-35032, Germany
SOURCE: Bioorganic & Medicinal Chemistry (2000), 8(3), 557-562
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GRAPHIC IMAGE:



I



II

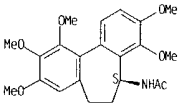


III

ABSTRACT:
Several B-ring variations of O-Me androbiphenyline, newly accessible from (-)-(M,7S)-colchicine via photo-oxygenation and subsequent endoperoxide-transformation, were synthesized and evaluated for their inhibitory effects on tubulin assembly in vitro. The amino-allocolchicinoid I, a key compound in this study, was transformed to the highly potent ketone and by oxidation with H2O2/Na2WO4 to a mixture of syn/anti-oximes. These could easily be transformed to hitherto unknown allocolchicinoids II and III with an eight membered B-ring lactam obtained via a Beckmann rearrangement. Surprisingly both do not notably affect tubulin assembly, despite obvious structural similarities with active analogs of the thiocolchicine- and azasteganacin-series.

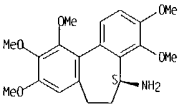
L4 ANSWER 6 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 266340-31-2 CAPLUS
CN 5H-Dibenzo[a,c]cyclohepten-5-amine, 6,7-dihydro-3,4,9,10,11-pentamethoxy-, (5S)- (9CI) (CA INDEX NAME)

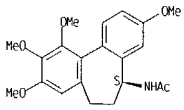
Absolute stereochemistry.



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

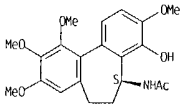
L4 ANSWER 6 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
IT 65967-01-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(allocolchicinoids with eight membered B-ring design, synthesis and inhibition of tubulin assembly)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 126223-60-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(allocolchicinoids with eight membered B-ring design, synthesis and inhibition of tubulin assembly)
RN 126223-60-7 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-4-hydroxy-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



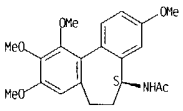
IT 129724-71-6P 266340-31-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(allocolchicinoids with eight membered B-ring design, synthesis and inhibition of tubulin assembly)
RN 129724-71-6 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,4,9,10,11-pentamethoxy-5H-

L4 ANSWER 7 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:13115 CAPLUS
DOCUMENT NUMBER: 132:189292
TITLE: Antitumor Agents. 199. Three-Dimensional Quantitative Structure-Activity Relationship Study of the Colchicine Binding Site Ligands Using Comparative Molecular Field Analysis
AUTHOR(S): Zhang, Shun-Xiang; Feng, Jun; Kuo, Sheng-Chu; Brossi, Arnold; Hamel, Ernest; Tropsha, Alexander; Lee, Kuo-Hsiung
CORPORATE SOURCE: Natural Products Laboratory and the Laboratory for Molecular Modeling School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC, 27599, USA
SOURCE: Journal of Medicinal Chemistry (2000), 43(2), 167-176
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Inhibitors of tubulin polymerization interacting at the colchicine binding site are potential anticancer agents. We have been involved in the synthesis of a number of colchicine site agents, such as thiocolchicinoids and allocolchicinoids, which are colchicine analogs, and 2-phenyl-quinolones and 2-aryl-naphthyridinones, which are the amino analogs of cytotoxic antimitotic flavonoids. The most cytotoxic of the latter compds. strongly inhibit binding of radiolabeled colchicine to tubulin, and these agents therefore probably bind in the colchicine site of tubulin. We have applied conventional CoMFA and q2-GRS CoMFA to identify the essential structural requirements for increasing the ability of these compds. to form tubulin complexes. The CoMFA model for the training set of 51 compds. yielded cross-validated R2 (q2) values of 0.637 for conventional CoMFA and 0.692 for q2-GRS CoMFA. The predictive power of this model was confirmed by successful activity prediction for a test set of 53 compds. with known potencies as inhibitors of tubulin polymerization. The activities of 88% of the compds. were predicted with absolute value of residuals of less than 0.5. The predictive q2 values were 0.546 for conventional CoMFA and 0.426 for q2-GRS CoMFA. The conventional CoMFA model with the highest predictive q2 (0.546) was analyzed in detail in terms of underlying structure-activity relationships.

IT 65967-01-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(QSAR study of colchicine binding site ligands using CoMFA)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

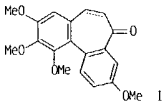
L4 ANSWER 7 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



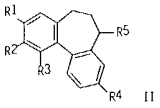
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:218951 CAPLUS
DOCUMENT NUMBER: 131:19161
TITLE: Antitumor agents. 192. Antitubulin effect and cytotoxicity of C(7)-oxygenated allocolchicinoids
AUTHOR(S): Guan, Jian; Zhu, Xiao-Kang; Brossi, Arnold; Tachibana, Yoko; Bastow, Kenneth F.; Verdier-Pinard, Pascal; Hamel, Ernest; McPhail, Andrew T.; Lee, Kuo-Hsiung
CORPORATE SOURCE: Natural Products Laboratory, Division of Medicinal Chemistry and Natural Products, School of Pharmacy, University of North Carolina at Chapel Hill, NC, 27599, USA
SOURCE: Collection of Czechoslovak Chemical Communications (1999), 64(2), 217-228
CODEN: CCCCAK; ISSN: 0010-0765
PUBLISHER: Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic
DOCUMENT TYPE: Journal
LANGUAGE: English
GRAPHIC IMAGE:



I



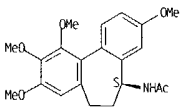
II

ABSTRACT:
Two allocolchicinoids (I) (bond single or double) prepared from colchicine together with allo compds. (II) (R1-R4 = OMe or OH, R5 = =O or H,OH) made from I by reduction and regiodemethylation, were evaluated for antitubulin and antitumor activities. Structures were confirmed by X-ray crystallog. anal. I and II have high tubulin binding affinity and display potent inhibitory activities against tubulin polymerization and solid human tumor cell lines. Particularly, drug-resistant KB cell lines, including KB-7d, KB-VCR, and KB-CPT, do not show marked resistance to these compds.

IT **65967-01-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antitubulin effect and cytotoxicity of C(7)-oxygenated allocolchicinoids)
RN 65967-01-3 CAPLUS

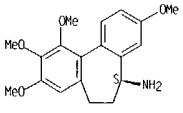
L4 ANSWER 8 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **84092-82-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antitubulin effect and cytotoxicity of C(7)-oxygenated allocolchicinoids)
RN 84092-82-0 CAPLUS
CN 5H-Dibenzo[a,c]cyclohepten-5-amine, 6,7-dihydro-3,9,10,11-tetramethoxy-, (5S)- (9CI) (CA INDEX NAME)

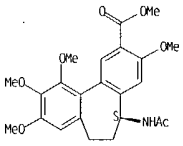
Absolute stereochemistry.



IT **94013-17-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis and antitubulin effect and cytotoxicity of C(7)-oxygenated allocolchicinoids)
RN 94013-17-9 CAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-2-carboxylic acid, 5-(acetylamino)-6,7-dihydro-3,9,10,11-tetramethoxy-, methyl ester, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 8 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

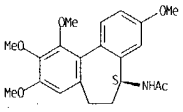


REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:474284 CAPLUS
DOCUMENT NUMBER: 129:149118
TITLE: Formaldehyde O-oxide and colchicine. An elegant route to the allocolchicines
AUTHOR(S): Dilger, Ulrich; Franz, Baerbel; Roettele, Herbert; Schroeder, Gerhard; Herges, Rainer
CORPORATE SOURCE: Institut Organische Chemie, Universitaet Karlsruhe, Karlsruhe, D-76128, Germany
SOURCE: Journal fuer Praktische Chemie/Chemiker-Zeitung (1998), 340(5), 468-471
CODEN: JPCCEM; ISSN: 0941-1216
PUBLISHER: Johann Ambrosius Barth
DOCUMENT TYPE: Journal
LANGUAGE: German
ABSTRACT:
Reactions of formaldehyde O-oxide with colchicine and its derivs. under O3-free conditions are reported. The fragmentation of intermediately formed spiro ozonides opens up an elegant route to allocolchicines. The fragmentation kinetics are described.

IT 65967-01-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of allocolchicines from formaldehyde oxide and colchicines)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

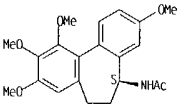
Absolute stereochemistry. Rotation (-).



L4 ANSWER 10 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
energetic contribution, while the effect of ring B is only entropic. It was concluded that both microtubule assembly inhibition and induction of GTPase activity were modulated by the same postbinding conformational change in tubulin. The difference between the strengths of these activities induced by ligands reflects the difference between a narrow allosteric effect between two well-defined sites in the case of GTPase activity and a broad effect aimed at the multiple sites involved in the incorporation of a tubulin protomer into the microtubule structure. Thus, there seems to be a loose thermodn. linkage between binding and GTPase activity, while there is none between binding and microtubule inhibition, the two phenomena being linked only kinetically.

IT 65967-01-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(role of linkages between components of colchicine and its biphenyl analogs in binding to tubulin, and preparation of colchicine analogs)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



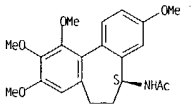
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:52223 CAPLUS
DOCUMENT NUMBER: 128:201984
TITLE: Linkages in Tubulin-Colchicine Functions: The Role of the Ring C (C') Oxygens and Ring B in the Controls
AUTHOR(S): Perez-Ramirez, Bernardo; Gorbunoff, Marina J.; Timasheff, Serge N.
CORPORATE SOURCE: Department of Biochemistry, Brandeis University, Waltham, MA, 02254-9110, USA
SOURCE: Biochemistry (1998), 37(6), 1646-1661
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Linkages between structural components of colchicine (COL) and its biphenyl analogs (allocolchicine, ALLO, and its analogs) in the binding to tubulin and its functional consequences were scrutinized. Three ring ALLO analogs with the carbomethoxyl in position 4' of ring C' replaced by a carbomethyl (KAC) and methoxy (MAC) groups were synthesized. The binding properties and consequences of binding (microtubule inhibition, abnormal polymerization, and induction of GTPase activity) were compared within the series of three ring and two ring compds., as well as between pairs consisting of a two ring and a three ring compound with identical groups in position 4'. Binding measurements showed that the binding of KAC to the COL binding site proceeded with similar chemical characteristics as that of its two ring analog (TKB), but with the kinetic characteristics of ALLO. The binding constant of KAC was found to be 1.9+106 M-1 and that of MAC was 4.6+105 M-1. The binding strength of the three ring analogs in descending order was KAC > ALLO > MAC, with increments similar to the biphenyl compds., TKB > TCB > TMB. The difference in binding affinities between the pairs of three ring and two ring mols. was invariant ($\delta\Delta G^\circ$ = -1.3±0.2 kcal/mol-1), showing that in all cases ring B makes only an entropic contribution by suppressing free rotation about the biaryl bond. In the case of microtubule inhibition, all three ring compds. inhibited strongly with similar potencies, even though the spread in inhibition strength between the corresponding two ring mols. was >3.3 kcal mol-1 of free energy. This difference was interpreted in terms of the ability of the various mols. to maintain tubulin in the proper conformation for binding in abnormal geometry to the growth end of a microtubule. This ability attains a maximal plateau value for three ring compds., independently of the oxygen-containing group in ring C' (or C) and is maintained for the Me ketone whether in a two or three ring compound The induction of the GTPase activity was found to follow in general the binding affinity, with the exception that mols. that contained a Me ketone were stronger GTPase inducers than expected from their alignment according to binding affinity. The finding that the binding of tropolone Me ether (ring C of COL) induced a GTPase activity shows that ring C contains the ability to induce both substoichiometric microtubule inhibition and GTPase activity. Rings A and B act only as anchors in the binding, with ring A making an

L4 ANSWER 11 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:711546 CAPLUS
DOCUMENT NUMBER: 128:13362
TITLE: Dihydrocolchicine 8,12-endoperoxide. A novel starting material for convenient syntheses of the allocolchicinoids N-acetylcolchinol O-methyl ether and androbiphenyline
AUTHOR(S): Brecht, Rene; Haenel, Frank; Seitz, Gunther
CORPORATE SOURCE: Pharmazeutisch-Chemisches Institut, Universitat Marburg, Marburg, D-35032, Germany
SOURCE: Liebigs Annalen/Recueil (1997), (11), 2275-2279
CODEN: LIARFV
PUBLISHER: Wiley-VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 128:13362
ABSTRACT:
Optically pure dihydrocolchicine-8,12-endoperoxide (I) is used as the starting material for the synthesis of some bioactive allocolchicinoids. Depending on the reaction conditions and reagents employed, different modifications of the C ring of colchicine are achieved. PPh3 deoxygenation of I leads to the well known N-acetylcolchinol O-Me ether (NCME, 40% yield from colchicine). Treatment of I with MeOH/CH2Cl2/silica gel provides the plant alkaloid androbiphenyline in a yield of 60% from colchicine. Et3N-catalyzed transformation of I yields (-)-colchicine-8,12-dione (17% yield), together with a mixture of interconverting tetracyclic hemiketals. In contrast previous results, the assignment of the absolute configuration of natural (-)-colchicine, and the prepared allo-congeners, should be (M,7S) or (aR,7S) instead of (aS,7S).

IT 65967-01-3P 126223-60-7P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and revised absolute configuration of allo-colchicinoids from hydrocolchicine endoperoxide)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

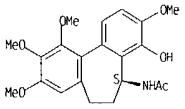
Absolute stereochemistry. Rotation (-).



RN 126223-60-7 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-4-hydroxy-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L4 ANSWER 11 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

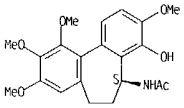


L4 ANSWER 12 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:303141 CAPLUS
DOCUMENT NUMBER: 127:34391
TITLE: Positional and facial selectivity in Diels-Alder reactions of (-)-(aS,7S)-colchicine. Synthesis of novel analogs of the alkaloid
AUTHOR(S): Brecht, Rene; Haenel, Frank; Seitz, Gunther; Frenzen, Gerlinde; Pilz, Astrid; Massa, Werner; Wocadlo, Sigrid
CORPORATE SOURCE: Pharmazeutisch-Chemisches Institut, Univ. Marburg, Marburg, D-35032, Germany
SOURCE: Liebigs Annalen/Recueil (1997), (5), 851-857
CODEN: LIARFV
PUBLISHER: VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 127:34391
ABSTRACT:
The positional and facial selectivity in Diels-Alder reactions of several hetero- and carbodienophiles with (-)-(aS,7S)-colchicine (I) was examined. In all cases, cycloaddn. occurred with high positional selectivity at the 8,12-positions of the alkaloid and preferentially from the diene face syn to the allylic substituent at the stereogenic center C(7). The observed high π-facial diastereoselectivity is independent of the polarity of the solvent used and is therefore probably a consequence of steric factors. The structures of Diels-Alder adducts of I with singlet O, N-phenyl-1,2,4-triazolinedione and trans-cyclooctene were assigned on the basis of spectral data and verified by x-ray crystallog.

IT **126223-60-7P**, Androbiphenyline
RL: BYP (Byproduct); PREP (Preparation)
(selectivity in Diels-Alder reactions of colchicine and preparation of analogs)
RN 126223-60-7 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-4-hydroxy-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

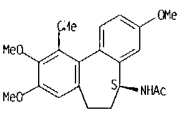


L4 ANSWER 13 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1995:326761 CAPLUS
DOCUMENT NUMBER: 122:150856
TITLE: Structure activity relationships in the colchicine molecule with respect to interaction with the mammalian multidrug transporter, P-glycoprotein
AUTHOR(S): Tang-Wai, David F.; Brossi, Arnold; Arnold, Lee D.; Gros, Philippe
CORPORATE SOURCE: Department of Biochemistry, McGill Univ., Montreal, QC, H3G 1Y6, Can.
SOURCE: Heterocycles (1994), 39(1), 385-403
CODEN: HTCYAM; ISSN: 0385-5414
PUBLISHER: Japan Institute of Heterocyclic Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Colchicine forms part of a group of structurally unrelated cytotoxic drugs to which P-glycoprotein overexpression confers resistance to, both in cultured cells in vitro and tumor cells in vivo. Modifications of the methoxy groups on the A and C rings modulated cellular toxicity but had no effect on P-glycoprotein interaction. Modifications at the C7 position of the B-ring, in particular the removal of the nitrogen atom of the acetamido group, had a dramatic effect. Examination of calculated molar refractivities (CMR) revealed that only compds. showing CMR values greater than 9.7 were P-glycoprotein substrates, suggesting a minimal size requirement for efficient interaction with P-glycoprotein.

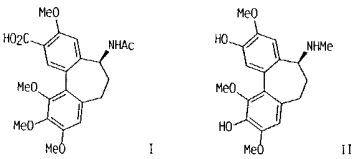
IT **65967-01-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structure activity relationships in the colchicine mol. with respect to cytotoxicity and interaction with mammalian multidrug transporter P-glycoprotein)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L4 ANSWER 14 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

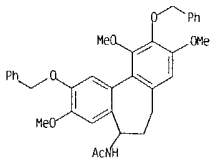
ACCESSION NUMBER: 1995:233412 CAPLUS
DOCUMENT NUMBER: 122:106200
TITLE: Total syntheses of the structures assigned to salimine and jerusalemine, alkaloids from Colchicum decaisnei Boiss. (Liliaceae)
AUTHOR(S): Banwell, Martin G.; Fam, Marie-Anne; Gable, Robert W.; Hamel, Ernest
CORPORATE SOURCE: School of Chemistry, Univ. of Melbourne, Victoria, 3052, Australia
SOURCE: Journal of the Chemical Society, Chemical Communications (1994), (22), 2647-9
CODEN: JCCCAT; ISSN: 0022-4936
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 122:106200
GRAPHIC IMAGE:



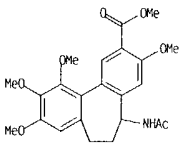
ABSTRACT:
Total syntheses of the dibenzo[a,c]cycloheptylamines (±)-I and (±)-II were developed; the spectroscopic properties of synthetic II match those reported for the alkaloid jerusalemine but compound I is different from the alkaloid salimine.

IT **160518-24-1P 160552-45-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total syntheses of the structures assigned to salimine and jerusalemine)
RN 160518-24-1 CAPLUS
CN Acetamide, N-[6,7-dihydro-3,9,11-trimethoxy-2,10-bis(phenylmethoxy)-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

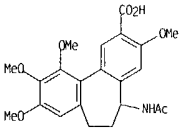
L4 ANSWER 14 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 160552-45-4 CAPLUS
CN 5H-Dibenzo[a.c]cycloheptene-2-carboxylic acid, 5-(acetylamino)-6.7-dihydro-3.9.10.11-tetramethoxy-, methyl ester (9CI) (CA INDEX NAME)

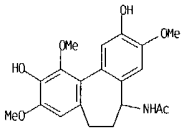


IT **160552-44-3P 160552-46-5P**, (±)-Jerusalemine
RL: SPN (Synthetic preparation): PREP (Preparation)
(total syntheses of the structures assigned to salimine and jerusalemine)
RN 160552-44-3 CAPLUS
CN 5H-Dibenzo[a.c]cycloheptene-2-carboxylic acid, 5-(acetylamino)-6.7-dihydro-3.9.10.11-tetramethoxy- (9CI) (CA INDEX NAME)

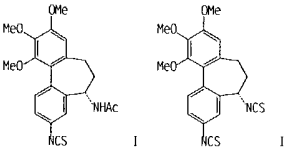


L4 ANSWER 14 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 160552-46-5 CAPLUS
CN Acetamide, N-(6.7-dihydro-2.10-dihydroxy-3.9.11-trimethoxy-5H-dibenzo[a.c]cyclohepten-5-yl)- (9CI) (CA INDEX NAME)



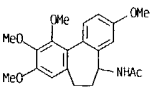
L4 ANSWER 15 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:604651 CAPLUS
DOCUMENT NUMBER: 117:204651
TITLE: Potential covalent markers of the colchicine-binding-site on turbulin: allocolchicinoids substituted in ring C or in rings B and C with isothiocyanato groups
AUTHOR(S): Boye, Olivier; Hamel, Ernest; Brossi, Arnold
CORPORATE SOURCE: Lab. Struct. Biol., NIDDK, Bethesda, MD, 20892, USA
SOURCE: Medicinal Chemistry Research (1991), 1(2), 142-50
CODEN: MCREEB; ISSN: 1054-2523
DOCUMENT TYPE: Journal
LANGUAGE: English
GRAPHIC IMAGE:



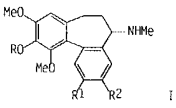
I II

ABSTRACT:
Isothiocyanates (I and II) were as active as colchicine as inhibitors of tubulin polymerization. A radiolabel can be introduced into the methoxy group at C-2 to ultimately afford radiolabeled I and II needed for further study.

IT **143956-83-6**
RL: BIOL (Biological study)
(tubulin polymerization inhibition by, colchicine binding site in relation to)
RN 143956-83-6 CAPLUS
CN Acetamide, N-(6.7-dihydro-3.9.10.11-tetramethoxy-5H-dibenzo[a.c]cyclohepten-5-yl)-, stereoisomer (9CI) (CA INDEX NAME)



L4 ANSWER 16 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:55514 CAPLUS
DOCUMENT NUMBER: 116:55514
TITLE: New natural dibenzocycloheptylamine alkaloids: a possible catabolic route for the colchicine alkaloids
AUTHOR(S): Abu Zarga, Musa H.; Sabri, Salim; Al-Tel, Taleb H.; Atta-ur-Rahman; Shah, Zahir; Feroz, M.
CORPORATE SOURCE: Chem. Dep., Univ. Jordan, Amman, Jordan
SOURCE: Journal of Natural Products (1991), 54(4), 936-40
CODEN: JNPRDF; ISSN: 0163-3864
DOCUMENT TYPE: Journal
LANGUAGE: English
GRAPHIC IMAGE:

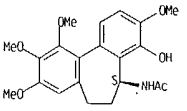


I

ABSTRACT:
Colchicum decaisnei of Jordanian origin yielded 3 new alkaloids (-)-jerusalemine (I, R = H, R1 = OH, R2 = OMe), (-)-salimine (I, R = Me, R1 = CO2H, R2 = OMe), and (-)-suhailamine (I, R = Me, R1 = H, R2 = CO2Me), besides the known alkaloid (-)-androbiphenyline.

IT **126223-60-7**, (-)-Androbiphenyline
RL: BIOL (Biological study)
(of Colchicum decaisnei)
RN 126223-60-7 CAPLUS
CN Acetamide, N-[(5S)-6.7-dihydro-4-hydroxy-3.9.10.11-tetramethoxy-5H-dibenzo[a.c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

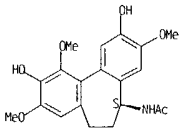
Absolute stereochemistry. Rotation (-).



IT **138704-11-7**, (-)-Jerusalemine **138704-12-8**, (-)-Salimine
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

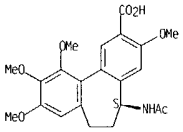
L4 ANSWER 16 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(of Colchicum decaisnei, isolation and mol. structure of)
RN 138704-11-7 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-2,10-dihydroxy-3,9,11-trimethoxy-5H-dibenzo[a,c]cycloheptен-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

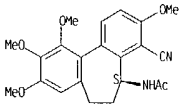


RN 138704-12-8 CAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-2-carboxylic acid, 5-(acetylamino)-6,7-dihydro-3,9,10,11-tetramethoxy-, (5S)- (9CI) (CA INDEX NAME)

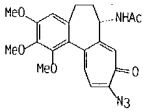
Absolute stereochemistry.



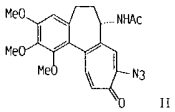
L4 ANSWER 17 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 17 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:43251 CAPLUS
DOCUMENT NUMBER: 114:43251
TITLE: Synthesis, photochemical decomposition, and tubulin binding of 10-azido-10-demethoxycolchicine and 9-azido-9-demethoxyisocolchicine
AUTHOR(S): Staretz, Marianne E.; Hastie, Susan Bane
CORPORATE SOURCE: Dep. Chem., State Univ. New York, Binghamton, NY, 13901, USA
SOURCE: Journal of Organic Chemistry (1991), 56(1), 428-32
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:43251
GRAPHIC IMAGE:



I



II

ABSTRACT:
Colchicine and isocolchicine analogs I and II were synthesized and studied as potential photoaffinity labels for the colchicine site on tubulin. Anal. of the products after photolysis in the absence of tubulin indicates that the reactive intermediate is a ketene rather than a nitrene. The intermediate ketene from I was trapped by the amide nitrogen regardless of solvent, while the photolysis of II produced products that were dependent on the nature of the solvent. In a non-nucleophilic solvent such as dioxane, the intermediate ketene of II underwent a Cope cyclization to form a colchicinol derivative Photolysis of the colchicine isomer in the presence of tubulin produced a small inhibition of colchicine binding to the protein, which may be indicative of covalent bond formation between I and tubulin.

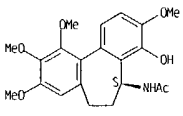
IT **129467-61-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 129467-61-4 CAPLUS
CN Acetamide, N-(4-cyano-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cycloheptен-5-yl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 18 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:548887 CAPLUS
DOCUMENT NUMBER: 113:148887
TITLE: New natural colchicinoids: indications of two possible catabolic routes for the colchicine alkaloids
AUTHOR(S): Al-Tel, Taleb H.; Abu Zarga, Musa H.; Sabri, Salim S.; Freyer, Alan J.; Shamma, Maurice
CORPORATE SOURCE: Dep. Chem., Pennsylvania State Univ., University Park, PA, 16802, USA
SOURCE: Journal of Natural Products (1990), 53(3), 623-9
CODEN: JNPRDF; ISSN: 0163-3864
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 113:148887
ABSTRACT:
Colchicum ritchii of Jordanian origin yielded 3 non-nitrogenous colchicinoids colchicone, 3-demethylcolchicone, and cornigerone, as well as the amidic (-)-colchibiphenyline, which in a solution in CDCl3 exists as a mixture of 2 isomers. The first 3 compds. may exemplify one catabolic route for the colchicine alkaloids, while (-)-colchibiphenyline, and the accompanying and previously known (-)-androbiphenyline may exemplify another.

IT **126223-60-7**
RL: BIOL (Biological study)
(from Colchicum ritchii, catabolism in relation to)
RN 126223-60-7 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-4-hydroxy-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cycloheptен-5-yl]- (9CI) (CA INDEX NAME)

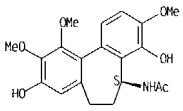
Absolute stereochemistry. Rotation (-).



IT **129724-65-8**, Colchibiphenyline
RL: BIOL (Biological study)
(from Colchicum ritchii, isolation and structure of, catabolism in relation to)
RN 129724-65-8 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-4,9-dihydroxy-3,10,11-trimethoxy-5H-dibenzo[a,c]cycloheptен-5-yl]- (9CI) (CA INDEX NAME)

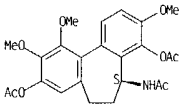
Absolute stereochemistry.

L4 ANSWER 18 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



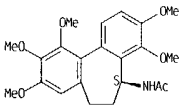
IT **129724-70-5P 129724-71-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 129724-70-5 CAPLUS
CN Acetamide, N-[4,9-bis(acetyloxy)-6,7-dihydro-3,10,11-trimethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

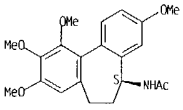


RN 129724-71-6 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,4,9,10,11-pentamethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

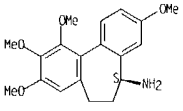


L4 ANSWER 19 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **128764-50-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation of)
RN 128764-50-1 CAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-5-amine, 6,7-dihydro-3,9,10,11-tetramethoxy-, hydrochloride, (S)- (9CI) (CA INDEX NAME)

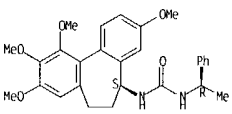
Absolute stereochemistry.



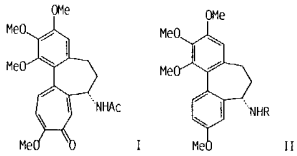
●HCl

IT **128764-49-8P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and crystal structure of)
RN 128764-49-8 CAPLUS
CN Urea, N-(6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl)-N'-(1-phenylethyl)-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 19 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:497860 CAPLUS
DOCUMENT NUMBER: 113:97860
TITLE: aS,7S-absolute configuration of natural (-)-colchicine and allo-congeners
AUTHOR(S): Brossi, Arnold; Boye, Olivier; Muzaffar, Anjum; Yeh, Herman J. C.; Toome, Voldemar; Wegrzynski, Bogda; George, Clifford
CORPORATE SOURCE: Lab. Struct. Biol., NIDDK, Bethesda, MD, 20892, USA
SOURCE: FEBS Letters (1990), 262(1), 5-7
CODEN: FEBLAL; ISSN: 0014-5793
DOCUMENT TYPE: Journal
LANGUAGE: English
GRAPHIC IMAGE:



I II

ABSTRACT:
The aS,7S-absolute configuration of (-)-colchicine (I) and (-)-N-acetylcolchinol Me ether (II, R = Ac), suggested on the basis of 1H-NMR data and neg. Cotton effects at about 260 nm (EtOH), is firmly established by an x-ray anal. of II [R = (R)-CONHCHMePh]. Binding of these compds. to tubulin requires an aS-configuration of the biaryl system.

IT **65967-01-3**
RL: PRP (Properties)
(absolute configuration of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

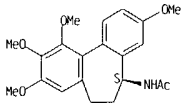
Absolute stereochemistry. Rotation (-).

L4 ANSWER 20 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:491051 CAPLUS
DOCUMENT NUMBER: 113:91051
TITLE: N-Acetylcolchinol O-methyl ether and thiocolchicine, potent analogs of colchicine modified in the C ring. Evaluation of the mechanistic basis for their enhanced biological properties
AUTHOR(S): Kang, Gil Jong; Getahun, Zelleka; Muzaffar, Anjum; Brossi, Arnold; Hamel, Ernest
CORPORATE SOURCE: Div. Cancer Treat., Natl. Cancer Inst., Bethesda, MD, 20892, USA
SOURCE: Journal of Biological Chemistry (1990), 265(18), 10255-9
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Two colchicine analogs with modifications only in the C ring are better inhibitors of cell growth and tubulin polymn than colchicine. Radiolabeled thiocolchicine (with a thiomethyl instead of a methoxy group at position C-10) and N-acetylcolchinol O-Me ether (NCME) (with a methoxy-substituted benzenoid instead of the methoxy-substituted tropone C ring) were prepared for comparison with colchicine. Scatchard anal. indicated a single binding site with KD values of 1.0-2.3 μM. Thiocolchicine was bound 2-4 times as rapidly as colchicine, but the activation energies of the reactions were nearly identical (18 kcal/mol for colchicine, 20 kcal/mol for thiocolchicine). NCME bound to tubulin in a biphasic reaction. The faster phase was 60 times as fast as colchicine binding at 37°, and a substantial reaction occurred at 0°. The rate of the faster phase of NCME binding changed relatively little as a function of temperature, so the activation energy was only 7.0 kcal/mol. Dissociation reactions were also evaluated, and at 37° the halflives of the tubulin-drug complexes were 11 min for NCME, 24 h for thiocolchicine, and 27 h for colchicine. Relative dissociation rates as a function of temperature varied little among the drug complexes. Activation energies for the dissociation reactions were 30 kcal/mol for thiocolchicine, 27 kcal/mol for NCME, and 24 kcal/mol for colchicine. Comparison of the activation energies of association and dissociation yielded free energies for the binding reactions of -20 kcal/mol for NCME, -10 kcal/mol for thiocolchicine, and -6 kcal/mol for colchicine. The greater effectiveness of NCME and thiocolchicine as compared with colchicine in biol. assays probably derives from their more rapid binding to tubulin and the lower free energies of their binding reactions.

IT **65967-01-3**
RL: BIOL (Biological study)
(as colchicine C ring-modified analog, tubulin binding of, enhancement of biol. activity in relation to)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

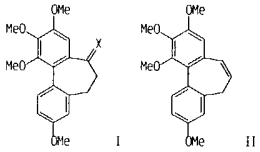
Absolute stereochemistry. Rotation (-).

L4 ANSWER 20 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 21 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1990:424296 CAPLUS
DOCUMENT NUMBER: 113:24296
TITLE: Deaminocolchinyl methyl ether: synthesis from 2,3,4,4'-tetramethoxybiphenyl-2-carbaldehyde. Comparison of antitubulin effects of deaminocolchinyl methyl ether and dehydro analogs
AUTHOR(S): Boye, Olivier; Itoh, Yoshikuni; Brossi, Arnold
CORPORATE SOURCE: NIDDK, NIH, Bethesda, MD, 20892, USA
SOURCE: Helvetica Chimica Acta (1989), 72(8), 1690-6
CODEN: HCACAV; ISSN: 0018-019X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 113:24296
GRAPHIC IMAGE:

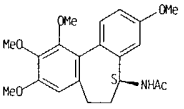


ABSTRACT:
Synthesis of deaminocolchinyl Me ether (I, X = H2) was achieved from the corresponding tetramethoxy-substituted biphenyl-2-carboxaldehyde via tricyclic ketone I (X = O) and 5,6-didehydro congener II. I (X = H2) was identical in every respect with material prepared from colchicine via the 6,7-didehydro congener. Measuring inhibition of tubulin polymerization in vitro showed the alloseries of colchicinoids, e.g. I (X = H2) and II, to be potent inhibitors.

IT 65967-01-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(inhibition by, of tubulin polymerization)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

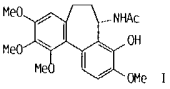
Absolute stereochemistry. Rotation (-).

L4 ANSWER 21 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 22 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

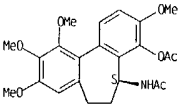
ACCESSION NUMBER: 1990:155179 CAPLUS
DOCUMENT NUMBER: 112:155179
TITLE: The dibenzocycloheptylamine alkaloids
AUTHOR(S): Tojo, Emilia; Abu Zarga, Musa H.; Freyer, Alan J.; Shamma, Maurice
CORPORATE SOURCE: Dep. Chem., Pennsylvania State Univ., University Park, PA, 16802, USA
SOURCE: Journal of Natural Products (1989), 52(5), 1163-6
CODEN: JNPRDF; ISSN: 0163-3864
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 112:155179
GRAPHIC IMAGE:



ABSTRACT:
Androcymbium palaestinum of Jordanian origin has yielded the new alkaloid (-)-androbiphenyline (I), which in CDCl3 solution exists as 2 conformers. Two previously known and related alkaloids are K-3 and K-4, obtained from a Colchicum species. I, K-3, and K-4 are the only known representatives of the dibenzocycloheptylamine class of alkaloids.

IT 126223-61-8
RL: PRP (Properties)
(conformation of)
RN 126223-61-8 CAPLUS
CN Acetamide, N-[4-(acetyloxy)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]-, (S)- (9CI) (CA INDEX NAME)

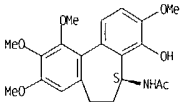
Absolute stereochemistry.



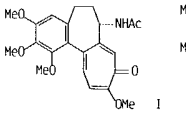
IT 126223-60-7
RL: BIOL (Biological study)
(from Androcymbium palaestinum, isolation and structure and conformation of)

L4 ANSWER 22 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 126223-60-7 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-4-hydroxy-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

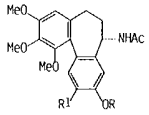
Absolute stereochemistry. Rotation (-).



L4 ANSWER 23 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1985:62488 CAPLUS
DOCUMENT NUMBER: 102:62488
TITLE: Contraction of the tropolonic ring of colchicine by hydrogen peroxide oxidation
AUTHOR(S): Iorio, Maria A.
CORPORATE SOURCE: Lab. Pharm. Chem., Ist. Super. Sanita, Rome, 00161, Italy
SOURCE: Heterocycles (1984), 22(10), 2207-11
CODEN: HTCYAM; ISSN: 0385-5414
DOCUMENT TYPE: Journal
LANGUAGE: English
GRAPHIC IMAGE:



I

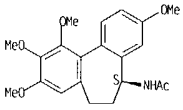


II

ABSTRACT:
Colchicine (I) underwent oxidative ring contraction by H2O2 to give the colchinols II (R = Me, R1 = H; R = H, R1 = CO2Me). The antimitotic activity of I and II were compared.

IT **65967-01-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and antimitotic activity of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

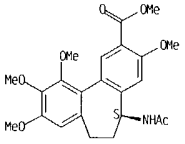
Absolute stereochemistry. Rotation (-).



IT **94013-17-9P**

L4 ANSWER 23 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 94013-17-9 CAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-2-carboxylic acid, 5-(acetylamino)-6,7-dihydro-3,9,10,11-tetramethoxy-, methyl ester, (5S)- (9CI) (CA INDEX NAME)

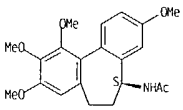
Absolute stereochemistry.



L4 ANSWER 24 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1983:72497 CAPLUS
DOCUMENT NUMBER: 98:72497
TITLE: Circular dichroism. LXVII. Isolation and chemistry of the alkaloids from the plants of the subfamily Wurmbaeoideae. XCII. Circular dichroism of alkaloids of colchicine type and their derivatives
AUTHOR(S): Hrbek, Jaromir, Jr.; Hruban, Ladislav; Simanek, Vilim; Santavy, Frantisek; Snatzke, Gunther; Yemul, Srishalam S.
CORPORATE SOURCE: Med. Fac., Palacky Univ., Olomouc, 775 15, Czech.
SOURCE: Collection of Czechoslovak Chemical Communications (1982), 47(8), 2258-79
CODEN: CCCCAK; ISSN: 0366-547X
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The CD spectra of 48 colchicine alkaloids and of some of their derivs. were given. The effects of the substituents and of the basic skeleton on the chiroptical properties of the measured compds. were discussed.

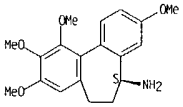
IT **65967-01-3 84092-82-0 84426-31-3**
RL: PRP (Properties)
(CD spectrum of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



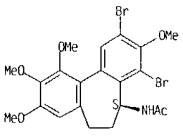
RN 84092-82-0 CAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-5-amine, 6,7-dihydro-3,9,10,11-tetramethoxy-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

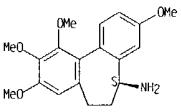


L4 ANSWER 24 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 84426-31-3 CAPLUS
CN Acetamide, N-(2,4-dibromo-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



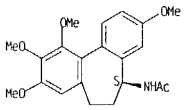
L4 ANSWER 25 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.



L4 ANSWER 25 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1983:27483 CAPLUS
DOCUMENT NUMBER: 98:27483
TITLE: Effect of colchicine derivatives on the antibody response induced in vitro
AUTHOR(S): Sterzl, J.; Santavy, F.; Sedmera, P.; Cudlin, J.
CORPORATE SOURCE: Inst. Microbiol., Czech. Acad. Sci., Prague, 142 20/4, Czech.
SOURCE: Folia Microbiologica (Prague, Czech Republic) (1982), 27(4), 256-66
CODEN: FOMIAZ; ISSN: 0015-5632
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The relation between structure and biol. activity of the title compds. (I) was investigated on isolated spleen cells of 3-mo-old female BALB/c mice cultivated with antigen, sheep red blood cells, and the number of antibody forming cells was determined by the plaque technique. Some I were toxic in vitro. Most compds. at concentration within the range of the immunoinhibitory effect, do not decrease the normal viability of lymphocytes; however, they prevent their conversion to the blastic form. Some I showed an immunoinhibitory effect at 0.001 μg/mL, whereas others were ineffective even at 10 μg/mL. There was no correlation between the I toxicity in mice, rats, and tissue culture (Santavy, F., 1958) and the immunoinhibitory effect on lymphocytes.

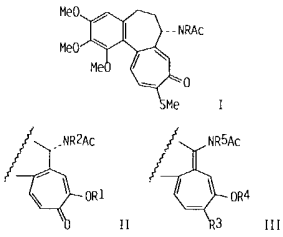
IT **65967-01-3 84092-82-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunosuppressant activity of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 84092-82-0 CAPLUS
CN 5H-Dibenzo[a,c]cyclohepten-5-amine, 6,7-dihydro-3,9,10,11-tetramethoxy-, (5S)- (9CI) (CA INDEX NAME)

L4 ANSWER 26 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1979:72367 CAPLUS
DOCUMENT NUMBER: 90:72367
TITLE: New chemistry of colchicine and related compounds. III. Reaction of thiocolchicine, isocolchicine and colchiceine with acetic anhydride
AUTHOR(S): Blade-Font, Artur
CORPORATE SOURCE: Res. Dep., Prod. Frumtost S. A., Barcelona, Spain
SOURCE: Afinidad (1978), 35(355), 239-41
CODEN: AFINAE; ISSN: 0001-9704
DOCUMENT TYPE: Journal
LANGUAGE: English
GRAPHIC IMAGE:

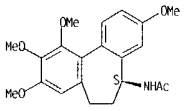


ABSTRACT:
Thiocolchicine (I; R = H) and isocolchicine (II; R1 = Me, R2 = H) reacted with boiling Ac2O to give non-tropolonic achiral enol acetates III (R3 = SMe, R4 = Ac; R3 = OAc, R4 = Me; R5 = Ac), resp. in moderate to 74% yields. Colchiceine (II; R1 = R2 = H) refluxed 70 h with Ac2O gave 84% II (R1 = Ac, R2 = H), 4.5% II (R1 = R2 = Ac), and 3% III (R3 = OAc, R4 = R5 = Ac). Acetolysis or basic hydrolysis of these derivs. regenerated the tropolonic rings to give the corresponding racemic colchicine-related compds. The transformation of colchicine-related products into achiral non-tropolonic enol esters by refluxing aliphatic anhydrides is facilitated by electron-releasing substituents in ring C and an acylamino group at C-7 is required for the reaction.

IT **65967-01-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(attempted reaction of, with acetic anhydride)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

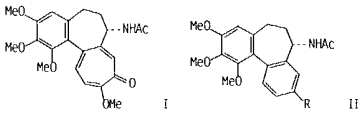
Absolute stereochemistry. Rotation (-).

L4 ANSWER 26 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 27 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1978:121468 CAPLUS
DOCUMENT NUMBER: 88:121468
TITLE: Benzoid rearrangement of colchicine in the presence of ethylene glycol
AUTHOR(S): Kiselev, V. V.; Perel'son, M. E.; Kikot, B. S.; Kostenko, O. S.
CORPORATE SOURCE: Onkol. Nauchn. Tsentr., Moscow, USSR
SOURCE: Zhurnal Organicheskoi Khimii (1977), 13(11), 2337-42
CODEN: ZORKAE; ISSN: 0514-7492
DOCUMENT TYPE: Journal
LANGUAGE: Russian
GRAPHIC IMAGE:

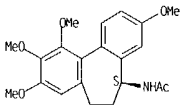


I II

ABSTRACT:
Rearrangement of colchicine (I) in refluxing HOCH2CH2OH gave deoxy- (II; R = H), O-(hydroxyethyl)-N-acetylcolchinol (II; R = HOCH2CH2O), and hydroxyethyl colchicinoate II (R = HOCH2CH2O2C). Structures were determined by NMR, IR, and UV spectroscopy.

IT **65967-01-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L4 ANSWER 27 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

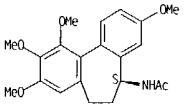
L4 ANSWER 28 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1964:493670 CAPLUS
DOCUMENT NUMBER: 61:93670
ORIGINAL REFERENCE NO.: 61:16351g-h
TITLE: Substances from the plants of the subfamily Wurmbaeoideae and their derivatives. LX. Optical rotations and rotatory dispersion of the colchicine alkaloids
AUTHOR(S): Hrbek, J., Jr.; Jennings, J. P.; Klyne, W.; Santavy, F.
CORPORATE SOURCE: Palacky Univ., Olomouc
SOURCE: Collection of Czechoslovak Chemical Communications (1964), 29(11), 2822-31
CODEN: CCCCAK; ISSN: 0010-0765
DOCUMENT TYPE: Journal
LANGUAGE: English

ABSTRACT:
cf. CA 61, 7357d. The monochromatic mol. optical rotations and the rotatory dispersion data of 23 compds. were determined in various solvents. The optical rotatory dispersion curves of colchicine, isocolchicine, colchinol-HCl, and N-acetylcholchinol in MeOH are charted and discussed.

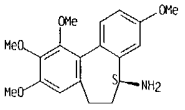
IT **65967-01-3**, Colchinol, N-acetyl-O-methyl- **84092-82-0**, Colchinol, O-methyl-
(optical rotation and rotatory dispersion of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 84092-82-0 CAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-5-amine, 6,7-dihydro-3,9,10,11-tetramethoxy-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

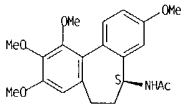


L4 ANSWER 28 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L4 ANSWER 29 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1964:38928 CAPLUS
DOCUMENT NUMBER: 60:38928
ORIGINAL REFERENCE NO.: 60:6889f-h
TITLE: Mass spectrometry in structural and stereochemical problems. XXXIII. Substances from the plants of the subfamily Wurmbaeoideae and their derivatives. 55. Colchicine alkaloids
AUTHOR(S): Wilson, J. M.; Ohashi, M.; Budzikiewicz, H.; Santavy, F.; Djerassi, Carl
CORPORATE SOURCE: Stanford University, Stanford, CA
SOURCE: Tetrahedron (1963), 19(12), 2225-31
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GRAPHIC IMAGE: For diagram(s), see printed CA Issue.
ABSTRACT:
cf. CA 60, 1215h; preceding abstract. Mass spectra were measured for N,N-dimethyldeacetylcolchicine (I, R = R' = Me), N-acetylcolchicinol Me ether, colchicine, I (R = H, R' = CHO), colchiceine, I (R = H, R' = Me), and γ-lumicolchicine (II), and correlations between spectra and structure made. The results indicate that mass spectra will be of assistance in structure determination of such naturally occurring tropolones.

IT **65967-01-3**, Colchinol, N-acetyl-O-methyl-, (mass spectrum of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

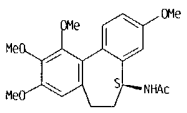
Absolute stereochemistry. Rotation (-).



L4 ANSWER 30 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1960:112375 CAPLUS
DOCUMENT NUMBER: 54:112375
ORIGINAL REFERENCE NO.: 54:21484h-i,21485a
TITLE: The effect of colchicine and some chemically related compounds on experimental viral infections
AUTHOR(S): Weinstein, Louis; Chang, Te-Wen
CORPORATE SOURCE: Tufts Univ., Boston, MA
SOURCE: Antibiotics and Chemotherapy (Washington, D. C.) (1960), 10, 180-7
CODEN: ANTCAO; ISSN: 0570-3123
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ABSTRACT:
Colchicine, cholchiceine, isocolchicine, aminocolchicide, butylaminocolchicide, and propylaminocolchicide, given to mice prior to infection with influenza or encephalomyocarditis virus increased slightly the time of onset of death but did not reduce the total number of fatalities. Acetylcolchinol, colchinol Me ether ditartrate, N-acetylcolchinol Me ether, dihydrodeaminocolchinol Me ether, N-acetylisocolchinol, 5-aminodibenzo[a,c] [1,3]-cycloheptadien-HCl, dibenzo [a,c][1,3]-cycloheptadien-5-one, and 10-acetamido-2,3,4,7-tetramethoxyphenanthrene have been found to alter the course of encephalomyocarditis infection in mice, mostly when given 2 days before or 1-2 days after initiation of infection.

IT **65967-01-3**, Colchinol, N-acetyl-O-methyl-, (effect on viral infections)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

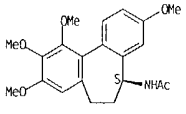
Absolute stereochemistry. Rotation (-).



L4 ANSWER 31 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1956:66029 CAPLUS
DOCUMENT NUMBER: 50:66029
ORIGINAL REFERENCE NO.: 50:12304f-g
TITLE: Substances in meadow saffron and their derivatives. Biological activity of colchicine derivatives in relation to their constitution
AUTHOR(S): Cernoch, M.; Malinsky, J.; Telupilora, O.; Santavy, F.
CORPORATE SOURCE: Palacky Univ., Olomouc, Czech.
SOURCE: Archives Internationales de Pharmacodynamie et de Therapie (1954), 99, 141-62
CODEN: AIPTAK; ISSN: 0003-9780
DOCUMENT TYPE: Journal
LANGUAGE: German
ABSTRACT:
cf. C.A. 45, 4343a. Colchicine and 88 derivs. were examined for acute toxicity and in many instances for their ability to produce mitotic arrest in metaphase in regenerating rat liver (stathmokinetic effect). The toxicity-stathmokinetic index varied from 1 to 10. The relation of structure to toxicity was discussed in detail.

IT **65967-01-3**, Colchinol, N-acetyl-, methyl ether, (pharmacology of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

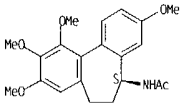
Absolute stereochemistry. Rotation (-).



L4 ANSWER 32 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1956:66028 CAPLUS
DOCUMENT NUMBER: 50:66028
ORIGINAL REFERENCE NO.: 50:12304e-f
TITLE: Comparison of the effect of thyroxine on basal metabolism and on oxidative phosphorylation
AUTHOR(S): Martius, Carl; Bieling, Hans; Nitz-Litzow, Dagobert
CORPORATE SOURCE: Univ. Wurzburg, Germany
SOURCE: Biochemische Zeitschrift (1955), 327, 163-9
CODEN: BIZEA2; ISSN: 0366-0753
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ABSTRACT:
The decrease in phosphorylation rate in the diaphragm and liver mitochondria of guinea pigs and rats has a definite relation to the increase in basal metabolism, and each can be calculated from the other. Thyroxine has a greater influence on the 1st step of oxidative phosphorylation than on the 2 following ones.

IT **65967-01-3**, Dibenzo[a,c][1.3]cycloheptadiene, 7-acetamido-1.2.3.9-tetramethoxy-
(pharmacol. of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6.7-dihydro-3.9.10.11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

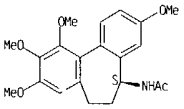


L4 ANSWER 33 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1956:19105 CAPLUS
DOCUMENT NUMBER: 50:19105
ORIGINAL REFERENCE NO.: 50:3895b-f
TITLE: Studies in light absorption. XIV. Steric effects in ortho-substituted diphenyls
AUTHOR(S): Braude, E. A.; Forbes, W. F.
CORPORATE SOURCE: Imperial Coll. Sci. Technol., London
SOURCE: Journal of the Chemical Society, Abstracts (1955) 3776-82
CODEN: JCSAAZ; ISSN: 0590-9791
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ABSTRACT:
On the basis of the 2 types of steric effects distinguished above (part XI), the contradictory interpretations of the extensive data in the literature on ortho-substituted biphenyls is reconsidered here. New data are reported for the o-alkylbiphenyls (cf. Goodman and Wise, C.A. 44, 10690b) and these absorption data are tabulated and discussed with those for the 2-HO, 2-MeO, 2-iodo, 2.2'-, 3.3'-, 4.4'-di-Me, di-HO, and di-MeO derivs. of biphenyl. All show steric effects of type 2, signifying nonplanar ground and excited states, and the hypsochromic shifts produced by 2 ortho substituents are approx. twice those produced by 1. Reasons are given for the contrast with analogous acetophenones and styrenes (parts XI and XIII), which show steric effects of type 1. Ortho-bridged biphenyls, on the other hand, show chiefly steric effects of type 1, signifying nonplanar ground and near-planar excited states. Values for λmaximum, εmaximum, ε/εO, and θ1 (the interplanar angle) are tabulated for fluorene, 9.10-dihydrophenanthrene (XXII), and its o.o'-di-Me and o.o'-di-MeO derivs., 2.7-dihydrodibenzoxepin (XXIII), and its o.o'-di-Me and o.o'-di-MeO derivs., N-acetylcolchinol methyl ether, 2.7-dihydrodibenzazepinium bromide and its o.o'-di-MeO derivative, and phenyldihydrothebaine (XXIV). Photographs of scale models of XXII and XXIII are included. Discussion of these data leads to the conclusion that the 2- and 3-membered ortho bridges impose a restriction on twist, and values of θ1 calculated as above are about 20° for XXII and XXIII in good agreement with those indicated by the models. Introduction of ortho substituents into short-bridged biphenyls increases θ1 to about 40°, whereas the 5-membered ortho bridge in XXIV permits a large twist, and θ1 calculated from the spectral data is greater than 60°. The discussion includes the different interpretation (on the basis, chiefly, of electronic interactions) of the absorption of biphenyls, especially XXIII and its derivs., by Turner (Beaven, et al., C.A. 49, 2382g), and reasons are given for preferring the present (steric) interpretation.

IT **65967-01-3**, Dibenzo[a,c][1.3]cycloheptadiene, 7-acetamido-1.2.3.9-tetramethoxy-
(spectrum of)
RN 65967-01-3 CAPLUS

L4 ANSWER 33 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Acetamide, N-[(5S)-6.7-dihydro-3.9.10.11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

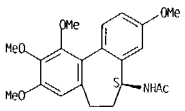
Absolute stereochemistry. Rotation (-).



L4 ANSWER 34 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1955:2320 CAPLUS
DOCUMENT NUMBER: 49:2320
ORIGINAL REFERENCE NO.: 49:515g-h
TITLE: Colchicine and colchicine-like compounds as chemotherapeutic agents
AUTHOR(S): Branch, Charles F.; Fogg, Lloyd C.; Ullyott, Glenn E.
SOURCE: Acta Unio Internationalis contra Cancrum (1949), 6, 439-47
CODEN: AICCA6; ISSN: 0365-3056
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ABSTRACT:
Colchicine, reduced colchicine, trimethylcolchicinic acid methyl ether α-tartrate (I), trimethylcolchicinic acid-HCl, N-acetylcolchinol (II), II-Me ether, colchinol-HCl, colchinol Me ether-HCl, N-benzoyltrimethylcolchicinic acid Me ether (III), 1-amino-2-phenyl-3-(3,4,5-trimethoxyphenyl)propane-HCl, 1-amino-2,3-diphenylpropane-HCl, and 1-amino-1,2-diphenylethane-HCl were examined for their effect on the mitotic rate of epithelium of mouse stomach. II and II-Me ether produced a moderate mitotic response. I, III, and colchicine produced the most marked mitotic response.

IT **65967-01-3**, Colchinol, N-acetyl-, methyl ether
(mitotic response to)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3.9.10.11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

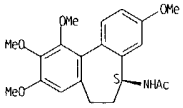
Absolute stereochemistry. Rotation (-).



L4 ANSWER 35 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1954:60406 CAPLUS
DOCUMENT NUMBER: 48:60406
ORIGINAL REFERENCE NO.: 48:10715e-h
TITLE: Substances from meadow saffron. XXH. Photochemical products of colchicine and derivatives
AUTHOR(S): Santavy, F.
CORPORATE SOURCE: Palacky Univ., Olomouc, Czech.
SOURCE: Biologicke Listy (1951), 31, 246-56
CODEN: BILIAC; ISSN: 0366-0486
DOCUMENT TYPE: Journal
LANGUAGE: Czech
ABSTRACT:
cf. C.A. 46, 126d; 45, 7750h. Irradiation of colchiceine, of N-acetylcolchinol Me ether, and of colchicinic acid with sunlight 5 years gave unchanged materials, together with small quantities of brown amorphous products. Colchicine also gave lumicolchicine I (I), C22H2506 (4 Me and a keto group), m. 184-6°, [α]20D 305° (c 0.783, CHCl3) (from AcOEt-Et2O) [oxime, m. 274-6° (from MeOH-Et2O)], (cf. C.A. 46, 126d). Intensive ultraviolet irradiation of 1 g. colchicine 20 hrs. in aqueous solution, extraction with CHCl3, and chromatography on Al2O3, gave 0.61 g. starting material, 0.20 g. I, 0.01 g. lumicolchicine II, C22H2506N (4 Me and a keto group), m. 276-8°, [α]27D -440° (c 0.820, CHCl3) (from AcOEt-Et2O) [oxime, m. 309-11° (from MeOH-Et2O)], identical with compound J, (C.A. 46, 9264c), and 0.13 g. amorphous material. Similar treatment of 5 g. compound E1 (C.A. 46, 126d) yielded 0.15 g. of a substance, m. 235-7° (oxime, m. 299-301°), identical with compound D (C.A. 46, 126d), and 0.004 g. of a substance m. 181-3°, different from I. I is identical with the "unstable" β-lumicolchicine of Grewe and W. Wulf (C.A. 46, 3544d). lumicolchicine II with γ-lumicolchicine.

IT **65967-01-3**, Colchinol, N-acetyl-, methyl ether
(light effect on)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

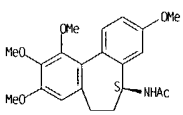


L4 ANSWER 35 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L4 ANSWER 36 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1954:60405 CAPLUS
DOCUMENT NUMBER: 48:60405
ORIGINAL REFERENCE NO.: 48:10715e-h
TITLE: Substances from meadow saffron. XXH. Photochemical products of colchicine and derivatives
AUTHOR(S): Santavy, F.
CORPORATE SOURCE: Palacky Univ., Olomouc, Czech.
SOURCE: Collection of Czechoslovak Chemical Communications (1951), 16, 665-75
CODEN: CCCCAK; ISSN: 0010-0765
DOCUMENT TYPE: Journal
LANGUAGE: German
ABSTRACT:
cf. C.A. 46, 126d; 45, 7750h. Irradiation of colchiceine, of N-acetylcolchinol Me ether, and of colchicinic acid with sunlight 5 years gave unchanged materials, together with small quantities of brown amorphous products. Colchicine also gave lumicolchicine I (I), C22H2506 (4 Me and a keto group), m. 184-6°, [α]20D 305° (c 0.783, CHCl3) (from AcOEt-Et2O) [oxime, m. 274-6° (from MeOH-Et2O)], (cf. C.A. 46, 126d). Intensive ultraviolet irradiation of 1 g. colchicine 20 hrs. in aqueous solution, extraction with CHCl3, and chromatography on Al2O3, gave 0.61 g. starting material, 0.20 g. I, 0.01 g. lumicolchicine II, C22H2506N (4 Me and a keto group), m. 276-8°, [α]27D -440° (c 0.820, CHCl3) (from AcOEt-Et2O) [oxime, m. 309-11° (from MeOH-Et2O)], identical with compound J, (C.A. 46, 9264c), and 0.13 g. amorphous material. Similar treatment of 5 g. compound E1 (C.A. 46, 126d) yielded 0.15 g. of a substance, m. 235-7° (oxime, m. 299-301°), identical with compound D (C.A. 46, 126d), and 0.004 g. of a substance m. 181-3°, different from I. I is identical with the "unstable" β-lumicolchicine of Grewe and W. Wulf (C.A. 46, 3544d). lumicolchicine II with γ-lumicolchicine.

IT **65967-01-3**, Colchinol, N-acetyl-, methyl ether
(light effect on)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

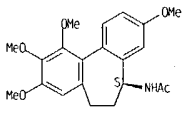
Absolute stereochemistry. Rotation (-).



L4 ANSWER 37 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1953:68162 CAPLUS
DOCUMENT NUMBER: 47:68162
ORIGINAL REFERENCE NO.: 47:11555f-h
TITLE: Enzyme changes induced in normal and malignant tissues with chemical agents. II. Effect of various compounds on the cytochrome oxidase activity of transplanted tumors
AUTHOR(S): Leiter, J.; Paradis, A. D.; Waravdekar, V. S.
CORPORATE SOURCE: Natl. Cancer Inst., Bethesda, MD
SOURCE: Journal of the National Cancer Institute (1940-1978) (1953), 14, 177-88
CODEN: JNCIAM; ISSN: 0027-8874
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ABSTRACT:
A single s.c. injection of tumor damaging agents (2 arsenicals, 2 antimonials, 2 phenazines, 1 quinoxaline, and 4 colchicines) in mice bearing sarcoma 37 produced a marked drop in cytochrome oxidase (I) within 24 h. A similar reduction in the I activity of tumor tissue homogenates was observed when some of these agents were injected into animals bearing lymphomas 1 and 2, leukemia 1210, mammary adenocarcinoma C3HBA, or melanoma S-91. In the case of lymphoma 2, spleen and lymph nodes which were heavily infiltrated with tumor showed a similar marked drop in I activity. Liver, whether from animals bearing this or other tumors, was little affected.

IT **65967-01-3**, Dibenzo[a,c][1.3]cycloheptadiene, 7-acetamido-1,2,3,9-tetramethoxy- **640735-77-9**, Colchinol, N-acetyliodo-, methyl ether
(effect on cytochrome oxidase in transplanted tumors)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

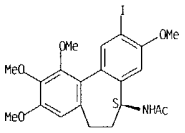
Absolute stereochemistry. Rotation (-).



RN 640735-77-9 CAPLUS
CN Colchinol, N-acetyliodo-, methyl ether (5CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 37 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



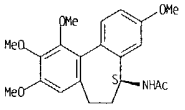
L4 ANSWER 38 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1953:22253 CAPLUS
DOCUMENT NUMBER: 47:22253
ORIGINAL REFERENCE NO.: 47:3843e-i,3844a
TITLE: Tribromocolchiceinic acid
AUTHOR(S): Lettre, Hans; Fernholz, Hans; Hartwig, Ernst
CORPORATE SOURCE: Univ. Heidelberg, Germany
SOURCE: Ann. (1952), 576, 147-54
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ABSTRACT:
cf. Windaus, C.A. 18, 3374; Cook, et al., C.A. 45, 2492f; and Rapoport, et al., C.A. 45, 10231i. Colchiceine (I) (1 g.) in 125 cc. CCl4 at 40° was treated slowly with 1 cc. Br, the mixture cooled to 0°, filtered, and the precipitate washed with CCl4, dried at 50° dissolved in 5 cc. AcOH, and treated with 0.5 cc. Br in 5 cc. AcOH, giving the compound (II), sintering 240°, m. 268° (termed "tribromocolchiceinic acid" by Windaus). When shaken in NaOH (3 cc. 0.1 N and later 5 cc. 2 N NaOH) with 1 cc. Me2SO4, 0.1 g. II gave 0.08 g. Me ester (III), m. 282° (decomposition). II in MeOH with CH2N2 in Et2O (cf. Schiele, Dissertation, University Gottingen, 1922) gave a "mono-Me derivative" of III, C23H24O7NBr3, m. 254°. II triturated with H2O and 2 N Na2CO3 gave, after warming at 80°, acidification, and cooling, IV (non ryst.), isolated and purified through the crystalline HCl salt, C20H20NO5Br3.HCl; Me ether of IV, m. 142° (from cyclohexane). The reduction of IV in AcOH with Zn dust (activated with Cu) gave N-acetylmonobromocolchinol (V), C20H22O5NBr, m. 202° (from AcOH). When the Zn dust reduction was carried out in 2 N NaOH, N-acetylcolchinol (VI), m. 148-9° (Me ether, m. 196-9°), was formed. IV with alkaline KMnO4 gave 3,4,5-trimethoxy-6-bromophthalic acid, m. 132°. I (1 g.) in 30 cc. 0.1 N KOH treated dropwise with 0.5 cc. Br and 5 cc. 40% KOH, then with SO2, and heated with H2O, gave 0.3 g. N-acetyldibromocolchinol (VII), C20H21O5NBr2, m. 226-8° (also given as 230°), which was also formed by brominating VI in 0.1 N NaOH. VII gave V, with Zn in acid and VI in alkaline solution KMnO4 and VII gave 3,4,5-trimethoxyphthalic anhydride, m. 143°. VI (0.25 g.) in aqueous NaOH treated 2 h. with 0.5 g. iodine, 2 g. KI, and 20 cc. H2O at room temperature and the excess iodine removed gave 0.3 g. of a N-acetylmonoiodocolchinol, m. 220-22° (also formed from I).

IT **65967-01-3**, Colchinol, N-acetyl-, methyl ether
(preparation of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L4 ANSWER 38 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

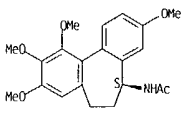


L4 ANSWER 39 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1953:10178 CAPLUS
DOCUMENT NUMBER: 47:10178
ORIGINAL REFERENCE NO.: 47:1851i,1852a-c
TITLE: Damage induced in sarcoma 37 with chemical agents. III. Colchicine derivatives related to trimethylcolchicinic acid and colchinol
AUTHOR(S): Leiter, J.; Downing, V.; Hartwell, J. L.; Shear, M. J.
CORPORATE SOURCE: Natl. Cancer Inst., Bethesda, MD
SOURCE: Journal of the National Cancer Institute (1940-1978) (1952), 13, 379-92
CODEN: JNCIAM; ISSN: 0027-8874
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ABSTRACT:
Derivs. (15) of colchicine (I) were examined in about 1500 mice for ability to damage sarcoma 37 following a single subcutaneous dose; 13 derivs. damaged the tumor at or below the maximum tolerated dose (MTD). Six had a ratio of MTD to min. effective dose (MED) of 4 or greater; the ratio for I was 2. Trimethylcolchicinic acid Me ether d-tartrate, trimethylcolchicinic acid Et ether d-tartrate, and N-acetylcolchinol had MTD/MED of 25. Minor changes in the substituents on I to form other derivs. of trimethylcolchicinic acid markedly altered the lethality and tumor-damaging potency. Changes in lethality were not always paralleled by equivalent changes in tumor-damaging potency. Degradation of the 7-membered C ring to a 6-membered aromatic ring did not abolish potency. Of 6 such compds., the MTD/MED for 4 was greater than for I. Compds. methylated in the 7-membered ring generally had higher relative potency than the unmethylated analogs. The methylated compds. were less potent than the unmethylated ones when the C ring was 6-membered. In 3 of 4 analogous pairs, the compds. containing a 6-membered aromatic C ring were more potent than their analogs with a 7-membered ring.

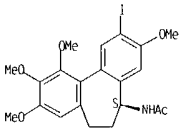
IT **65967-01-3**, Colchinol, N-acetyl-, methyl ether **640735-77-9**
, Colchinol, N-acetyliodo-, methyl ether
(sarcoma 37 damaging capacity of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 640735-77-9 CAPLUS
CN Colchinol, N-acetyliodo-, methyl ether (5CI) (CA INDEX NAME)

L4 ANSWER 39 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.

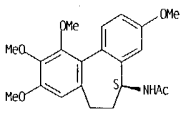


L4 ANSWER 40 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1952:11446 CAPLUS
DOCUMENT NUMBER: 46:11446
ORIGINAL REFERENCE NO.: 46:2041e-i,2042a-c
TITLE: Colchicine and related compounds. XI. Synthesis of N-acetylcolchinol methyl ether
AUTHOR(S): Cook, J. W.; Jack, J.; Loudon, J. D.; Buchanan, G. L.; MacMillan, J.
CORPORATE SOURCE: Univ. Glasgow, UK
SOURCE: Journal of the Chemical Society, Abstracts (1951) 1397-1403
CODEN: JCSAAZ; ISSN: 0590-9791
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ABSTRACT:
cf. C.A. 44, 6872a. 2.3.4.7-Tetramethoxy-10-phenanthroic acid (C.A. 39, 2988.6) through the Me ester yields the hydrazide (I), m. 216° (phenylsulfonyl derivative, m. 230-1°). I (5.7 g.) in 80 cc. (CH2OH)2, treated with 3.6 g. anhydrous Na2CO3 and after 80 sec. diluted with 100 cc. boiling H2O, gives 2.3.4.7-tetramethoxy-10-phenanthraldehyde (II), m. 130°. II (1.1 g.) and 4 cc. 99% N2H4.H2O in 40 cc. EtOH, refluxed 2 hrs., give a yellow solid which, intimately mixed with 2 g. powdered KOH at 120-5° and heated 5-10 min., gives 2.3.4.7-tetramethoxy-10-methylphenanthrene, m. 134-5°. 9-Methylphenanthrene (2 g.) and 3 g. OsO4 in 15 cc. C6H6, treated with 2.4 cc. C5H5N, kept 7 days, the precipitate in CHCl3 shaken 2 hrs. with 50 g. mannitol and 2 g. KOH in 200 cc. H2O, gives cis-9,10-dihydro-9, 10-dihydroxy-9-methylphenanthrene (III), m. 130-1°; 0.1 g. III and 0.21 g. Pb(OAc)4 in 20 cc. C6H6, shaken 2 hrs. and refluxed 0.5 hr., give 3,4:5,6-dibenzo-1,3,5-cycloheptatrien-7-one, m. 83-4°; the oxime (m. 190°). hydrogenated (1.5 hrs.) in Ac2O over Pt oxide, gives 2-acetamido-3,4:5,6-dibenzo-3,5-cycloheptadiene, m. 233°. In the preparation of the "B"-series of compds. as reported in C.A. 38, 5820.2, it is found that 2.3.4.5-tetramethoxy-9-phenanthraldehyde m. 101° (reported 92°) and 2,3,4,5-tetramethoxy-9-methylphenanthrene (IV) m. 116-17° (reported 102°); this may be a case of polymorphism. cis-9,10-Dihydro-9,10-dihydroxy-2,3,4,7-tetramethoxy-10-methylphenanthrene (V) m. 155-6°; with Pb(OAc)4 in C6H6 (shaken 2 hrs.), V yields 9,12,13,14-tetramethoxy-3,4:5,6-dibenzo-1,3,5-cycloheptatriene-7-one, m. 109-10°, which is identical with the ketonic oxidation product of desaminocolchinol Me ether; a by-product is a cream compound, m. 208-9°. 2,3,4,5-Tetramethoxy-9-methylphenanthrene yields cis-9,10-dihydro-9,10-dihydroxy-2,3,4, 5-tetramethoxy-9-methylphenanthrene (VI), m. 215-16°; with Pb(OAc)4 in C6H6, VI yields 6'-acetyl-6-formyl-2,2',3,4-tetramethoxybiphenyl (VII), m. 113-14°; dioxime, m. 179-80°. VII (10.6 g.) in 50 cc. MeOH, treated with a few drops of dilute NaOH, gives (after 4 days) 7-hydroxy-11,12,13,14-tetramethoxy-3,4:5,6-dibenzo-3, 5-cycloheptadien-2-one (VIII), m. 179-80°. VIII (0.1 g.), 0.6 cc. C5H5N, and 0.4 cc. Ac2O, heated 1 hr. at 100° and the cooled solution poured into dilute H2SO4 at 0°, give 11,12,13,14-tetramethoxy-

L4 ANSWER 40 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
3,4:5,6-dibenzo-3, 5, 7-cycloheptatrien-2-one, m. 174-5°. IV (1.3 g.) with OsO4 in C6H6-C5H5N give 0.9 g. cis-9,10-dihydro-9,10-dihydroxy-2,3,4,7-tetramethoxy-9-methylphenanthrene (IX), m. 172-4°. With Pb(OAc)4, VIII gives a gum which could not be crystd. but with NH2OH yields the dioxime, m. 186-7°. of 6,2,3,4-OCH(MeO)3C6H2C6H3(OMe)Ac-4, 6; cyclization with AcOH satd. with HCl gives 9,12,13,14-tetramethoxy-3,4:5,6-dibenzo-3,5,7-cycloheptatrien-2-one (X), yellow, m. 98-9°; hydrogenation of X in AcOH (0.5 hr. over Pd black) gives 9,12,13,14-tetramethoxy-3,4:5,6-dibenzo-3,5-cycloheptadien-2-one, m. 142-3°; oxime (XI), m. 203-4° (Rapoport, et al., C.A. 44, 10722f). XI, hydrogenated (4 hrs.) over Raney Ni at 80-90°/65-75 atm., gives (±)-colchinol Me ether (XII), m. 144-6° (Ac deriv., m. 179-80). (-)Colchinol Me ether [H (+)-6,6'-dinitrodiphenate], with 1 mol. MeOH, pale yellow, m. 257-8° (decompn.). [α]590016 51°, [α]549116 67° (MeOH, c 0.33); NaOH gives (-)-XII, m. 90-2° (picrate, m. 223-5°). (-)-XII is identical with that obtained by the degradation of colchicine.

IT **65967-01-3**, Dibenzo[a,c][1,3]cycloheptadiene, 7-acetamido-1,2,3,9-tetramethoxy-
(preparation of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

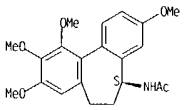
Absolute stereochemistry. Rotation (-).



L4 ANSWER 41 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1951:60097 CAPLUS
DOCUMENT NUMBER: 45:60097
ORIGINAL REFERENCE NO.: 45:10231i,10232a-i,10233a-g
TITLE: The synthesis of dl-colchinol methyl ether
AUTHOR(S): Rapoport, Henry; Williams, Arthur R.; Cisney, Merle E.
CORPORATE SOURCE: Univ. of California, Berkeley
SOURCE: Journal of the American Chemical Society (1951), 73, 1414-21
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 45:60097
ABSTRACT:
cf. C.A. 44, 10722e. Methylation of 2,5-O2N(HO)C6H3CHO yielded 25% 5-MeO compound (I), m. 82-3°. 3,4,5-(MeO)3C6H2CO2H and 2,5 mol SOCl2 in C6H6 yielded 91% acid chloride (II), b2.5 155-60°, m. 77-9° (from C6H6-MeEt). II and Pd-on-BaSO4 with S-quinoline poison yielded 81% of the aldehyde (III), via the bisulfite addition compound (IV). NaHSO3 (53.5 g.) in 194 cc. water added to 74.6 g. III yielded IV in 10 min.; water to form a thin paste and then 600 cc. Et2O were added, the mixture cooled in an ice bath, 46.6 g. NaCN in 114 cc. water added, the mixture stirred 30 min., 5.5 g. NaHSO3 added, the layers separated, the aqueous layer extracted with two 150-cc. portions of Et2O, and the Et2O evaporated from the combined exts., yielding 82 g. cyanohydrin (V), m. 99.6-100.8°. Hot AcOH and concentrated HCl (108 cc. each) containing 108 g. SnCl2 added to 74.0 g. V, the mixture stirred 3 h. under N in a boiling water bath, filtered hot, concentrated in vacuo to 0.25 volume, the concentrate poured into 1 l. saturated NaCl, and the mixture cooled overnight yielded 45 g. (plus 9 more from the mother liquor) 3,4,5-trimethoxyphenylacetic acid (VI), m. 117-18° (from water). VI (38.5 g.), 33.9 g. III, 52.3 g. Ac2O, and 17.2 g. Et3N heated 16 h. at 90-5°, 10 cc. water added at room temperature, the mixture poured after 1 h. into 1.1 l. water containing 160 g. K2CO3 and heated on the steam bath, the solution washed with C6H6, then Et2O, filtered through C, and acidified with concentrated HCl yielded 55.6 g. 2-nitro-5-methoxy-α-(3,4,5-trimethoxyphenyl)cinnamic acid (VII), m. 157-9°. VII (17.7 g.) in 1:1 warm water and concentrated NH4OH (60 cc.) added to 315 cc. concentrated NH4OH and 370 cc. water at 75° containing 120 g. FeSO4.7H2O, the precipitate allowed to settle, filtered after 1 h., washed 4 times with dilute NH4OH, and the filtrate cooled and adjusted to pH 3.3 with concentrated HCl yielded 14.1 g. amino acid (VIII), m. 189-91° (from EtOH). Concentrated H2SO4 (7.7 cc.) added with stirring to 35.5 g. VIII in 700 cc. dioxane, the mixture cooled to room temperature, 16.3 g. iso-AmNO2 added, the mixture stirred 1 h., the diazonium salt added during 30 min. to 200 cc. 6.8 M NaH2PO2 containing 6 g. Gattermann Cu paste [Ber. 23, 1218(1890)] at 50-60°, the mixture poured into 4 l. water containing 80 cc. concentrated NH4OH, filtered through C, and the filtrate acidified with concentrated HCl yielded 21.1 g. 2,3,4,7-tetramethoxy-10-phenanthrenecarboxylic acid (IX), m. 201-2°; Me ester, m. 104-5°. IX (1.9 g.), 16 cc. quinoline, and 0.1 g. CuSO4 heated 3 h. at 200-10° yielded 1.45 g. 2,3,4,7-tetramethoxyphenanthrene (X), sublimate recrystd. from EtOH, m. 151-2°; picrate, deep red needles, m. 123-3.5°. IX (25 g.), 18.3 g. SOCl2, and 300 cc. C6H6 refluxed 1 h. yielded 25.4 g. acid chloride (XI), m. 162-4° (from C6H6). NaN3 (4.8 g.) in 18 cc. water added to XI in 2 l. Me2CO (ice bath), the solution allowed to stand 15 min., 6 l.

L4 ANSWER 41 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
water added during 30 min., the azide filtered off and refluxed 1 h. in 300 cc. abs. EtOH. 300 cc. 4 N EtOH-KOH added, the mixt. refluxed 4 h., filtered, and the filtrate cooled yielded 19.2 g. 2,3,4,7-tetramethoxy-10-phenanthrylamine (XII), m. 153.5-54° (from abs. EtOH). One run with excessive water present yielded 6.5% 1,3-bis(2,3,4,7-tetramethoxy-10-phenanthryl)urea (XIII), m. 277.6-278°. XIII with KOH in (CH2OH)2 heated 18 h. at 150° yielded 64% XII. XII heated 5 min. on the steam bath with a 2-fold excess of Ac2O yielded the N-Ac deriv., m. 226-8°. IX (1.20 g.) yielded 19% of the phenanthrenequinone (XIV), m. 195-6°. Oxidn. of X yielded traces of XIV; XII yielded 24%. XII (20.0 g.), 200 cc. dioxane, and 200 cc. water satd. with SO2 at 0°, heated in sealed tubes 48 h. at 100-5° yielded 18.5 g. 2,3,4,7-tetramethoxy-10-phenanthrol (XV), m. 167-9° (from aq. EtOH). XV and Me2SO4 yielded 2,3,4,7,10-pentamethoxyphenanthrene, m. 111-12°. XV (19.7 g.) in 90 cc. N KOH and 5 g. NaNO2 in 40 cc. water mixed and cooled to 0°, 240 cc. N H2SO4 added during 1 h. (temp. at 3-5°), and the mixt. stirred 30 min. and filtered yielded 18.0 g. 2,3,4,7-tetramethoxyphenanthrenequinone 9-oxime (XVI), m. 154-5°, solidified and m. 173-5°. XVI (20 g.), 11.4 g. PhSO2Cl, and 160 cc. pyridine refluxed 1.5 h., cooled, added to 800 cc. 6 N HCl, cooled in an ice bath, filtered, 100 cc. 2 N K2CO3 added to the ppt. in 500 cc. MeOH, the soln. refluxed 1 h., 100 cc. water added, and the MeOH evapd. on the steam bath yielded 15.2 g. 2-(2-cyano-4-methoxyphenyl)-3,4,5-trimethoxybenzoic acid (XVII), m. 216.5-18° (from 10:1 C6H6-Pr2). XVII (0.3 g.) boiled 24 h. with 1 g. KOH in 50 cc. water yielded 0.24 g. 2'-carboxy acid, m. 240-1°. XVII (10.6 g.), 20 g. SOCl2, and 150 cc. C6H6 refluxed 1 h., the SOCl2 evapd. with C6H6, 2.2 g. Pd-on-BaSO4 and 0.2 cc. S-quinoline poison added to the acid chloride in 150 cc. xylene, the soln. filtered after 4 h., the filtrate concd. in vacuo, the residue in 300 cc. MeOH refluxed 1 h. with 100 g. 40% NaHSO3, and the addn. compd. decompd. with satd. Na2CO3 yielded 6.8 g. 2-(2-cyano-4-methoxyphenyl)-3,4,5-trimethoxybenzaldehyde (XVIII), m. 92-2.5°; semicarbazone m. 222-3° (from aq. EtOH). XVIII (12.9 g.), 8.2 g. CH2(CO2H)2, 40 cc. pyridine, and 0.8 cc. piperidine heated 30 min. at 80°, 2 h. at 100° refluxed 30 min., and the cooled soln. poured slowly into 200 cc. 6 N HCl (ice bath) yielded 13.5 g. of the cinnamic acid, (MeO)3[NC(MeO)C6H3]C6CH:CHCO2H (XIX), m. 224-5°. Hydrogenation of the Na salt of XIX with Pd-on-C yielded β-[2-(2-cyano-4-methoxyphenyl)-3,4,5-trimethoxyphenyl]propionic acid (XX), m. 124.5-5.5° (from aq. EtOH); amide (from the acid chloride), m. 170-1° (from C6H6). The Na salt from 6 g. XIX hydrogenated 30 min. at room temp. and pressure with 1.2 g. 5% Pd-on-C yielded 5.3 g. β-[2-(2-carboxy-4-methoxyphenyl)-3,4,5-trimethoxyphenyl]propionic acid (XXI), m. 175-6.5° (from MeOH-water 1:2). XXI (4.5 g.), 35 cc. MeOH, and 1.5 cc. concd. H2SO4 refluxed 18 h. yielded 4.6 g. di-Me ester (XXII), m. 110-11° (from aq. MeOH). XXII (4.4 g.) in 75 cc. PhMe added during 2 h. to 1.24 g. K in 10 cc. refluxing PhMe contg. 5 drops MeOH, the mixt. refluxed 11 h., cooled, 5 cc. and then 50 cc., water added, the PhMe layer washed, dried, and the PhMe evapd. yielded crude 1,2,3,9-tetramethoxy-6-carbomethoxydibenzo[a,c] [1,3] cycloheptadiene-7-one

L4 ANSWER 41 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 41 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(XXIII); 5 g. KOH in 10 cc. water added to XXIII in 90 cc. MeOH, the mixt. allowed to stand overnight at room temp., refluxed 1 h., 15 cc. concd. HCl added, the soln. refluxed overnight, 100 cc. water added, the MeOH evapd., the ketone extd. with CHCl3 and washed with water. NaOH, and water yielded 2.4 g. 1,2,3,9-tetramethoxydibenzo[a,c] [1,3]cycloheptadien-7-one (XXIV), m. 140.5-41° (from MeOH); semicarbazone, m. 246-6.5° (from CHCl3-EtOH); oxime, m. 194-6° (from MeOH). XXIV (0.5 g.), 0.35 g. KOH, 6.0 cc. (CH2OH)2, and 0.3 cc. 85% N2H4.H2O heated according to Huang-Minlon (C.A. 41, 1649a), the cooled mixt. dild. with 8 cc. water, acidified with concd. HCl, extd. with three 10-cc. portions of C6H6, the exts. washed, the C6H6 evapd., the residue shaken 2 h. at room temp. with 35 cc. 3 N NaOH and 5 cc. Me2SO4, the mixt. extd. with C6H6 (3 + 10 cc.) the C6H6 evapd., and the residue in 5 cc. MeOH filtered through C yielded 0.29 g. 1,2,3,9-tetramethoxydibenzo[a,c][1,3]cycloheptadiene (XXV), m. 96-8°. Hydrogenation of XXIV oxime yielded 0.43 g. 7-amino-1,2,3,9-tetramethoxydibenzo[a,c][1,3]cycloheptadiene (XXVI) (dl-colchinol Me ether); HCl salt, m. 258-9°; N-Ac deriv. (XXVII) m. 178-9° (from 1:1 aq. MeOH). Colchicine (XXVIII) was converted to colchiceine and thence to N-acetyliodocolchinol (XXIX) (Windaus, C.A. 9, 1481). XXVIII (5% in MeOH contg. 3 equivs. of NaOH) hydrogenated at room temp. and pressure yielded 90% N-acetylcolchinol, which with CH2N2 yielded N-acetylcolchinol Me ether (XXIX), m. 201-2°, [α]20D -86.6 (c 0.67, MeOH). XXIX (3 g.) in 30 cc. MeOH, and 30 cc. concd. HCl refluxed 24 h. yielded 2.5 g. colchinol Me ether (XXX) HCl salt, m. 258-9°, [α]20D -88.7° (c 0.76, EtOH). d-Tartaric acid (1.62 g.) in 5 cc. water added to 1.77 g. XXX in 5 cc. warm water yielded the d-acid tartrate, m. 182-4°, [α]20D -62.2° (c 1.2, water) (from water). XXX (1.0 g.) and 0.5 g. BzH in 5 cc. MeOH warmed 15 min. yielded N-benzylidenecolchinol Me ether (XXXI), m. 145-6°, [α]25D 23.3° (c 0.73, dioxane). XXIX by the method of Cook, et al. (C.A. 38, 5819.2), yielded desaminocolchinol Me ether, hydrogenated to the dihydro compd. XXXI (0.60 g.) refluxed 5 h. in 5 cc. of 35% MeOH-PhCH2Me3NOH yielded dl-XXX, m. 258-9°, 0° rotation; N-Ac deriv., m. 180-1°; alone or mixed with XXVII.

IT 65967-01-3, Colchinol, N-acetyl-, methyl ether
(preparation of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

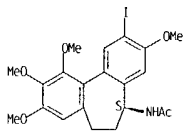
L4 ANSWER 42 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1951:33365 CAPLUS
DOCUMENT NUMBER:	45:33365
ORIGINAL REFERENCE NO.:	45:5804b-d
TITLE:	Effects of mitotic inhibitors on tumor cells
AUTHOR(S):	MacCardle, Ross C.
CORPORATE SOURCE:	Natl. Cancer Inst., Bethesda, MD
SOURCE:	Annals of the New York Academy of Sciences (1951), 51, 1489-96 CODEN: ANYAA9; ISSN: 0077-8923
DOCUMENT TYPE:	Journal
LANGUAGE:	Unavailable

ABSTRACT:
N-Acetyliodocolchinol methyl ether induces translocation of Fe from peripheral cytoplasm to midregion in sarcoma 37 cells arrested in metaphase, and accumulation of Ca and(or) Mg in the spindle area as revealed by microincineration. Podophyllin in low doses over a short period of time induces essentially the above changes. The most diverse agents can provoke similar alterations in mitosis; the effect seems to be governed by dose. It is felt that none of the changes found in chemically treated sarcoma 37 cells is peculiar to any particular chemical agent studied.

IT 640735-77-9, Colchinol, N-acetyliodo-, methyl ether
(effect on tumor cells)
RN 640735-77-9 CAPLUS
CN Colchinol, N-acetyliodo-, methyl ether (5CI) (CA INDEX NAME)

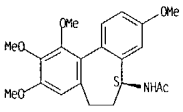
Absolute stereochemistry.



L4 ANSWER 43 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1951:29598 CAPLUS
DOCUMENT NUMBER: 45:29598
ORIGINAL REFERENCE NO.: 45:5123h-i,5124a-g
TITLE: The oxidation of phenol ethers with organic peroxy acids
AUTHOR(S): Fernholz, Hans
CORPORATE SOURCE: Univ. Heidelberg, Germany
SOURCE: Chemische Berichte (1951), 84, 110-22
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ABSTRACT:
In connection with some work on colchicine (I) (C.A. 45, 6871b), it has been found that phenol ethers (II) which generally are stable toward oxidation reagents are readily oxidized by BzO2H. II treated with 1-3% BzO2H-C6H6 4-7 days at 5-10° take up the following amts. of O atoms: PhOMe 0.5; p-MeC6H4OMe 0.6; 3,4-Me2C6H3OMe 3.1; 1,2,3,4-tetrahydro-2-naphthyl Me ether 3.1; 1-C10H7OMe (III) 2.8; 1-C10H7OEt (IV) 3.1; 2-C10H7OMe (V) 3.3; 2-C10H7OEt (VI) 3.1; 2-phenanthryl Me ether (VII) 2.9; 3-isomer (VIII) 3.3; p-MeOC6H4CH2CHPhNHAc 2.9; p-MeOC6H4CH2CH2CHPhNHAc 3.4; 3,5,4-RR'(MeO)C6H2CH2CH2CH[C6H4R''(P)]NHAc (IX) (R = R' = H, R'' = MeO) 5.9; veratrole 0.2; 3,4-(MeO)2C6H3Me 2.1; 1,2-C10H6(OMe)2 2.4; 5,6-dimethoxyhydrindene 4.1; IX (R = R'' = H, R' = MeO) 4.1; IX (R = H, R' = R'' = MeO) 5.8; 1,2,3-(MeO)3C6H3 4.7; 3,4,5-(MeO)3C6H2CH2CH2NHAc 4.7; IX (R = R' = MeO, R'' = H) 4.8; N-acetylcolchinol benzoate 4.6; allocolchiceine Et ether 4.6; IX (R = R' = R'' = MeO) 7.6; N-acetylcolchinol Me ether 7.8. Treating 6 g. V with 692 cc. 2.5% BzO2H in anhydrous C6H6 14 days at 10°, extracting the mixture exhaustively with aqueous NaHCO3, and acidifying the aqueous extract with HCl give a crystalline precipitate (X). Extracting the filtrate with CHCl3, evaporating the dried CHCl3 extract, and extracting the residue together with X in a Soxhlet with petr. ether give a mixture of BzOH and 2.75 g. o-HO2CC6H4CH:CHCO2Me (XI), m. 103-4°, separated by fractional sublimation. From the residue in the extraction thimble 0.15 g. o-HO2CC6H4CH:CHCO2H (XII), m. 198°, is isolated. Saponification of XI gives XII. Heating XII above its m.p. gives 3-phthalideacetic acid, m. 151°. Oxidation of 1 g. XI with KMnO4 in 3% NaHCO3 with warming gives 0.5 g. o-C6H4(CO2H)2. From the original C6H6 solution after extraction with NaHCO3 0.2 g. 2-methoxy-1,4-naphthoquinone (XIII), lemon-yellow needles, m. 181-2°, is isolated by chromatographic purification. Treating 3 g. V in 30 cc. EtOH with 290 cc. 3% BzO2H in C6H6 gives 0.9 g. o-HO2CC6H4CH:CHCO2Et (XIV), m. 95°, and 0.1 g. XIII. Addition of 20 cc. H2O to 3 g. V in 290 cc. 3% BzO2H in C6H6 and keeping the mixture 14 days at 10° gives 2.2 g. XII. VI (4 g.) with 440 cc. 2.2% BzO2H gives 1.3 g. XIV and 0.2 g. 2-ethoxy-1,4-naphthoquinone (XV), m. 120°. 2-C10H7OH (4 g.) in 30 cc. MeOH and 420 cc. 3% BzO2H give 1.5 g. XI; with EtOH in lieu of MeOH 1.3 g. XIV is obtained. III (4 g.) and 500 cc. 2.2% BzO2H give 1.1 g. XI and 0.9 g. 1,4-naphthoquinone (XVI), m. 124-5°. III and 290 cc. 3% BzO2H in 20 cc. EtOH give 0.9 g. XIV; with H2O in lieu of EtOH 1.5 g. XII is obtained. 1-C10H7OH (4 g.) and 420 cc. 3% BzO2H in 20 cc. MeOH give 1.1 g. XI. Keeping 2.5 g. VII with 260 cc. 2% BzO2H 16 days at 8-10° gives 1.2 g. Me 2-carboxy-1-naphthaleneacrylate, m. 148-9°, sapond. to the free acid (XVII), m. 187-8°. Warming 300 cc. AcOH with 30 cc. perhydrol 5 hrs. at 70° and keeping the mixt. 2 days at 20° give 2-2.5% AcO2H solns. Keeping 6 g. V with 470 cc. 2.25% AcO2H 14 days at 20° gives 3.2 g. XII; the filtrate, evapd. in vacuo to 1/3 its vol. and dild. with 2 vols. H2O, gives a ppt., sepd. with NaHCO3 into 1 g. XII and 1.4 g. XIII. Evapn. of the 2nd filtrate and treatment of the residue with NaHCO3 give another 0.6 g. XII and 0.3 g. XIII. Oxidation of 3 g. V in 80 cc. MeOH with 240 cc. 2.3% AcO2H gives 1.3 g. XI and 0.12 g. XIII. The following II are similarly oxidized: 4 g. VI with 280 cc. 2.28% AcO2H, giving 2.8 g. XII and 0.3 g. XV; the same in 80 cc. MeOH gives 1.6 g. XI; 4.5 g. 2-C10H7OCH2Ph and 240 cc. 2.28% AcO2H give 2.3 g. XII and 0.9 g. 2-benzyloxy-1,4-naphthoquinone, m. 144°; 3 g. V and 250 cc. 2.2% AcO2H give 1.4 g. XII and 0.6 g. XVI. Keeping 0.95 g. VII with 60 cc. 2.4% AcO2H 3 weeks at 20° gives 0.6 g. XVII. Oxidation of 4 g. VIII with 250 cc. 2.4% AcO2H 3 weeks at 20° gives 2 g. of an acid, m. 160°, which seems to be 1-carboxy-2-naphthaleneacrylic acid. Keeping 4 g. 1,2-naphthoquinone in 40 cc. MeOH with 120 cc. 4% perphthalic acid 8 days at 10° gives 1.8 g. XI. The reaction mechanisms of these oxidations and their significance regarding the structure of I are discussed.

IT **65967-01-3**, Dibenzo[a,c][1.3]cycloheptadiene, 7-acetamido-1,2,3,9-tetramethoxy-
(spectrum of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

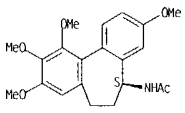
Absolute stereochemistry. Rotation (-).



L4 ANSWER 43 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

IT **65967-01-3**, Dibenzo[a,c][1.3]cycloheptadiene, 7-acetamido-1,2,3,9-tetramethoxy-
(oxidation of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L4 ANSWER 44 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1951:16564 CAPLUS
DOCUMENT NUMBER: 45:16564
ORIGINAL REFERENCE NO.: 45:2959b-d
TITLE: Colchicine. Nature of the B-ring
AUTHOR(S): Horowitz, R.; Ullyot, G. E.; Horning, E. C.; Horning, M. G.; Koo, J.; Fish, M. S.; Parker, J. A.; Walker, G. N.
CORPORATE SOURCE: Univ. of Pennsylvania, Philadelphia
SOURCE: Journal of the American Chemical Society (1950), 72, 4330-2
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ABSTRACT:
The UV absorption spectra for dihydrodeaminocolchinol Me ether, N-acetylcolchinol Me ether (I), and colchinol Me ether (II) are given; the behavior of II on acidification of the basic solution indicates that acylamino or amino substitution on the B ring does not significantly influence the UV absorption. Since the Ac group of I can be hydrolyzed without alteration of the B ring, it would appear that the 7-membered B ring is also present in colchicine. The absorption spectrum of Cook's carbinol (C.A. 34, 2851.3) indicates that this alc. is not derived from the ring system represented by I and II. The spectra for 2,3,4,7-tetramethoxyfluorene, m. 97-7.5°, and the 9-(2-hydroxyethyl) derivative, m. 100-1°, are given. The spectral characteristics suggests that the 3-membered bridge does not introduce a major hindrance to the assumption of coplanarity by the A-C rings in the colchinol series.

IT **65967-01-3**, Dibenzo[a,c][1.3]cycloheptadiene, 7-acetamido-1,2,3,9-tetramethoxy-
(spectrum of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

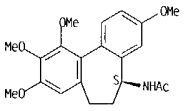
Absolute stereochemistry. Rotation (-).

L4 ANSWER 45 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1951:16563 CAPLUS
DOCUMENT NUMBER: 45:16563
ORIGINAL REFERENCE NO.: 45:2958f-i,2959a-b
TITLE: Synthesis of racemic β-Δ6-dihydrodesoxycodeine methyl ether
AUTHOR(S): Gates, Marshall; Tschudi, Gilg
CORPORATE SOURCE: Univ. of Rochester, Rochester, NY
SOURCE: Journal of the American Chemical Society (1950), 72, 4839-40
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GRAPHIC IMAGE: For diagram(s), see printed CA Issue.
ABSTRACT:
cf. C.A. 45, 1089c. 3,4-Dimethoxy-9,10-dioxo-4b-cyanomethyl-4b,5,8,8a,9,10-hexahydrophenanthrene (C.A. numbering), hydrogenated over Cu chromite, gives the keto lactam (I), m. 263-4.5°, absorption maximum at 281 mμ (log ε 4.16); Wolff-Kishner reduction and remethylation give the lactam (II), m. 210-12.5°, absorption maximum at 282 mμ (log ε 3.17); reduction with LiAlH4 and methylation with HCHO-HCO2H give the racemic base (III), an oil (picrate, m. 198.5-200°). β-Dihydrothebainone on hydrogenation yields the corresponding alc., m. 165.5-6°, [α]30D -23° (c 0.92) (methiodide, m. 264-5°); Me ether, m. 152.5-3.5°, [α]31D -9° (EtOH, c 0.643) (methiodide, m. 243-5°; picrate, m. 190-1°); reaction with p-MeC6H4SO2Cl and detosylation with boiling collidine give β-Δ6-dihydrodesoxycodeine Me ether (IV), an oil (picrate, m. 210-12°); the prefix β refers to the configuration at C14, epimeric with that of morphine. Dihydrothebainol yields a Me ether, an oil, [α]27D -28° (EtOH, c 1.519) (methiodide, m. 279-81°; HBr salt, m. 254.5-5°, [α]28D 34° (EtOH), c 0.447)); the tosylate (methiodide, m. 165-6°) yields an isomer of IV, an oil, which was purified through the fumarate, m. 233-5°. The infrared spectra of III and IV are virtually superimposable; that of the isomer is similar but shows certain differences. This synthesis proves that the point of attachment of the ethanamine side chain in the morphine alkaloids is at C13.

IT **65967-01-3**, Dibenzo[a,c][1.3]cycloheptadiene, 7-acetamido-1,2,3,9-tetramethoxy-
(spectrum of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

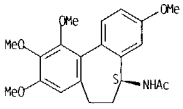
L4 ANSWER 45 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 46 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1951:13906 CAPLUS
DOCUMENT NUMBER: 45:13906
ORIGINAL REFERENCE NO.: 45:2492f-h
TITLE: Synthesis of (±)-N-acetylcolchinol methyl ether
AUTHOR(S): Cook, J. W.; Jack, J.; Loudon, J. D.
CORPORATE SOURCE: Univ., Glasgow, UK
SOURCE: Chemistry & Industry (London, United Kingdom) (1950) 650
CODEN: CHINAG; ISSN: 0009-3068
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ABSTRACT:
cf. C.A. 43, 2986d; Rapoport, et al., C.A. 44, 10722e. 2,3,4,7-Tetramethoxy9-methylphenanthrene was oxidized with OsO4 to the 9,10-dihydroxy-9,10-dihydro compound (I), m. 173-4°, which with Pb(OAc)4 gave a keto aldehyde (dioxime, m. 186-7°) cyclized by HCl in glacial HOAc to 9,12,13,14-tetramethoxy-3,4,5,6-dibenzocycloheptа-1,3,5-trien-2-one (II). II was hydrogenated over Pt black to the saturated ketone (III), m. 142-3° (from MeOH). The oxime of III, m. 203-4° (from MeOH), was hydrogenated over Raney Ni at 80-90° and 65-75 atmospheric to crude (±)-colchinol Me ether, m. 142-6° (HCl salt, m. 254°), which was acetylated to (±)-N-acetylcholchinol Me ether (IV), m. 179-80°.

IT 65967-01-3, Colchinol, N-acetyl-, methyl ether
(preparation of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

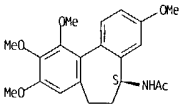
Absolute stereochemistry. Rotation (-).



L4 ANSWER 47 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1950:56404 CAPLUS
DOCUMENT NUMBER: 44:56404
ORIGINAL REFERENCE NO.: 44:10722e-i
TITLE: Synthesis of dl-colchinol methyl ether
AUTHOR(S): Rapoport, Henry; Williams, Arthur R.; Cisney, Merle E.
CORPORATE SOURCE: Univ. of California, Berkeley
SOURCE: Journal of the American Chemical Society (1950), 72, 3324-5
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ABSTRACT:
The following synthesis establishes the structure of colchinol Me ether as 7-amino-1, 2, 3, 9-tetramethoxydibenzo[a,c][1, 3]cycloheptadiene (I). 2, 3, 4, 7-Tetramethoxy-10-phenanthroic acid, through the Curtius degradation, yields 2, 3, 4, 7-tetramethoxy-10-phenanthrylamine, m. 153.5-4°; heated with SO2, it gives 2, 3, 4, 7-tetramethoxy-10-phenanthrol, m. 167-9°; HNO2 transforms this into 2, 3, 4, 7-tetramethoxyphenanthrenequinone 9-oxime, m. 173-5°, which with PhSO2Cl in C5H5N gives 2-(2-cyano-4-methoxyphenyl)-3, 4, 5-trimethoxybenzoic acid, m. 216.5-18°; by the methods used earlier (C.A. 43, 8377d), this was transformed into the cyano aldehyde (m. 92-2.5°), the cyanocinnamic acid (m. 224-5°), and (by hydrogenation and hydrolysis) the carboxypropionic acid (II), m. 175-6.5°. Hydrolysis of the intermediate β-keto acid formed by cyclization of the di-Me ester of II yields 1, 2, 3, 9-tetramethoxydibenzo[a,c] [1, 3]cycloheptadien-7-one, m. 140.5-1°; Wolff-Kishner reduction gives dihydrodeaminocolchinol Me ether (oxime, m. 194-6°); reduction gives dl-I (HCl salt, m. 258-9°; N-Ac derivative, m. 180-1°). I (HCl salt, m. 258-9°, [α]D20 -88.7° (EtOH, c 0.76); N-Ac derivative, m. 201-2°, [α]D20 -86.6° (MeOH, c 0.67); N-benzylidene derivative (III), m. 145-6°), was racemized by heating III with Me3(PhCH2)NOH in MeOH, followed by hydrolysis, giving dl-I (as HCl salt).

IT 65967-01-3, Colchinol, N-acetyl-, methyl ether
(preparation of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

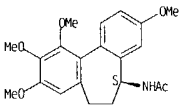
Absolute stereochemistry. Rotation (-).



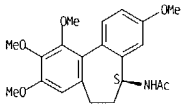
L4 ANSWER 48 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1950:35858 CAPLUS
DOCUMENT NUMBER: 44:35858
ORIGINAL REFERENCE NO.: 44:6871b-i
TITLE: Rearrangement of colchicine with sodium alcoholate and the structure of the C-ring
AUTHOR(S): Fernholz, Hans
CORPORATE SOURCE: Univ., Gottingen, Germany
SOURCE: Ann. (1950), 568, 63-72
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GRAPHIC IMAGE: For diagram(s), see printed CA Issue.
ABSTRACT:
F. substantiated Santavy's results (C.A. 42, 5891a), obtaining similar conversion products from colchicine (I). However, to avoid confusion, F. proposes the term allocolchiceine (II) for S's "acid colchique" [which is not identical with Zeisel's "colchicinic acid," Monatsh. 9, 1(1888)] and the term allocolchicine (III) for the Me ester of II (which is isomeric with I). Heating 0.5 g. carefully purified I 0.5 hr. with 3 cc. dry MeOH and 0.05 g. Na with exclusion of H2O gave about 0.47 g. III, m. 248° (from MeOH or C6H6), also formed quantitatively by heating 5 g. 18 days with 0.01 g. Na and 30 cc. dry MeOH. Crude I, or the presence of traces of H2O, lowered the yields of III and in the latter case gave II as well as III. I (5 g.) refluxed 1 hr. with 40 cc. 10% NaOH in ordinary MeOH, diluted with H2O, and acidified, gave about 4.5 g. II, m. 254-5° (after crystallization from MeOH and sublimation in a high vacuum to remove solvents). From NaOEt and I in EtOH was formed the Et ester of II, m. 216° (also obtained by transesterification of III). The Pr ester of II, m. 192° (from C6H6-petr. ether), was formed from NaOPr and I, by the transesterification of III, or by the direct esterification of II. III (1.8 g.) was heated 2 hrs. with 20 cc. HBr solution in glacial AcOH (d. 1.42), diluted, concentrated on the steam bath, treated with aqueous NaOH, filtered, the brown filtrate acidified with aqueous H2SO4, the resulting precipitate boiled 3 hrs. with 160 cc. H2O, 5 cc. 2 N NaOH, and 6 g. KMnO4, acidified with H2SO4, treated with SO2 to bleach the solution, saturated with Na2SO4, and extracted with Et2O, the dried, evaporated extract gave trimellitic acid anhydride (IV), m. 163° (after crystallization from Et2O-C6H6, and vacuum sublimation); free acid, m. 217-220° (on the Cu block). IV was also formed by oxidizing III with 12% HNO3 in AcOH, followed by treatments similar to those outlined above. Possible structures for the C-ring, especially the 7-membered ring proposed by Dewar (C.A. 39, 2067,3) and supported by Arnstein, et al. (C.A. 43, 8376b), are fully discussed. To 1 g. II in 10 cc. concentrated H2SO4 and 50 cc. CHCl3 at 40-45°, NaN3 was added very gradually, the mixture, poured into ice H2O, made alkaline, extracted exhaustively with CHCl3, and the extract evaporated and treated with aqueous H2SO4, giving the H2SO4 salt, m. 183-4°, of the corresponding free base, C20H24O4N2 (V), m. 255-6° (from very dilute MeOH); Bz derivative of V, m. 287° (from aqueous EtOH). Diazotization of V followed by heating gave Windaus' N-acetylcolchinol, m. 150° (from EtOH); Me ether, m. 199° (cf. Windaus, Sitzber. heidelberg. Akad. Wiss., Math.-naturw. Klasse, Abt. A, 16, Abh. (1919)). The C-ring in III therefore appears to have the structure IIIc and it is evident that the structure of the C-ring (VI) in I as suggested by Windaus is untenable.

L4 ANSWER 48 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
IT **65967-01-3**. Colchinol, N-acetyl-, methyl ether
(preparation of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L4 ANSWER 49 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 49 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1950:30187 CAPLUS
DOCUMENT NUMBER: 44:30187
ORIGINAL REFERENCE NO.: 44:5887h-i,5888a-d
TITLE: Effect of hydrogen peroxide in alkaline medium on colchiceine
AUTHOR(S): Cech, J.; Santavy, F.
CORPORATE SOURCE: Palacky Univ., Olomouc
SOURCE: Collection of Czechoslovak Chemical Communications (1949), 14, 532-9
CODEN: CCCCAK; ISSN: 0010-0765
DOCUMENT TYPE: Journal
LANGUAGE: English
GRAPHIC IMAGE: For diagram(s), see printed CA Issue.
ABSTRACT:
By the action of H_2O_2 in alkaline solution on colchiceine (I) were obtained N-acetylcolchinol (II) and an amorphous product. From the reaction mixture obtained on methylation with Me_2SO_4 or CH_2N_2 was isolated N-acetylcolchinol Me ether (III). On the basis of this data, the C-ring of Dewar's formula for I (Nature 155, 479(1945)) should have the substituents located as shown in formula I. I (1 g.), m. 140-6°, in an equivalent amount of 0.1 N NaOH and of 30% H_2O_2 was held at 60° for 6 h., the mixture cooled (crystals, m. 140-8°, may be filtered off at this point), acidified to litmus with 1% HCl, extracted with $CHCl_3$, the $CHCl_3$ evaporated, and the residue (IV) crystallized from MeOH-H_2O. Chromatog. of IV on alkali-free Al_2O_3, with $CHCl_3$-EtOH (92:8) as solvent, gave II, m. 213-15°, $[\alpha]D20$ -51.6 ± 2°, which gave no color with $FeCl_3$ and did not reduce polarog. II (50 mg.) in 10 mL. MeOH treated with ethereal CH_2N_2 for 0.5 h. gave a product, m. 201-3° (sublimation) (from EtOAc-Et_2O), identical with an authentic sample of III. Crude IV (2 g.) was shaken 4 h. in 100 mL. 10% NaOH and 10 mL. Me_2SO_4 and extracted with $CHCl_3$; evaporation of the $CHCl_3$ gave III, m. 204-6° (from aqueous MeOH). III was also obtained by methylation of IV with CH_2N_2 and chromatog. (on Al_2O_3) of the product; the other reaction products were amorphous and not identified.

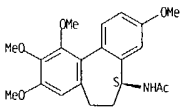
IT **65967-01-3**. Colchinol, N-acetyl-, methyl ether
(preparation of)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L4 ANSWER 50 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1948:37073 CAPLUS
DOCUMENT NUMBER: 42:37073
ORIGINAL REFERENCE NO.: 42:7880c-e
TITLE: Histologic criteria for evaluating the capacity of chemical agents to produce damage rapidly in sarcoma 37
AUTHOR(S): MacCardle, Ross C.; Downing, Virginia
CORPORATE SOURCE: Natl. Cancer Inst., Bethesda, MD
SOURCE: Cancer Research (1947), 7, 717
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ABSTRACT:
The necrosis-producing capacity of chemical agents on implanted sarcoma 37 was ascertained by injecting single doses subcutaneously into mice and observing the extent and speed of changes in cells of tumor and intestinal epithelium fixed in Zenker's formol-dichromate fluid at 8, 20, and 48 hrs. after administration. Histological effects are described of N-acetyliodocochinol Me ether (Compound 368), a quaternary ammonium salt (Compound 707), α-phenyl-β-(3,5-diiodo-4-hydroxyphenyl)propionic acid (Compound 497), and podophyllin (Agent 85V); all injured the tumor cells. Podophyllin interfered with mitosis in sarcoma, epidermis, and intestine cells of mice, produced necrosis in Rous sarcoma of chickens, and damaged cerebellar Purkinje cells in chickens.

IT **65967-01-3**, Dibenzo[a,c][1,3]cycloheptadiene, 7-acetamido-1,2,3,9-tetramethoxy- **640735-77-9**, Colchinol, N-acetyliodo-, methyl ether
(necrosis by)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

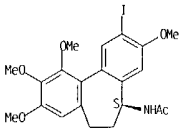
Absolute stereochemistry. Rotation (-).



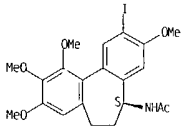
RN 640735-77-9 CAPLUS
CN Colchinol, N-acetyliodo-, methyl ether (5CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 50 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 51 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



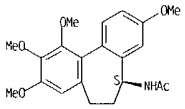
L4 ANSWER 51 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1948:37072 CAPLUS
DOCUMENT NUMBER: 42:37072
ORIGINAL REFERENCE NO.: 42:7880c-e
TITLE: Histologic criteria for evaluating the capacity of chemical agents to produce damage rapidly in sarcoma 37
AUTHOR(S): MacCardle, Ross C.; Downing, Virginia
CORPORATE SOURCE: Natl. Cancer Inst., Bethesda, MD
SOURCE: Am. Assoc. Cancer Research. 38th Ann. Meeting (1947), Volume Date 16 May 1947-17 May 1947
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ABSTRACT:

The necrosis-producing capacity of chemical agents on implanted sarcoma 37 was ascertained by injecting single doses s.c. into mice and observing the extent and speed of changes in cells of tumor and intestinal epithelium fixed in Zenker's formol-dichromate fluid at 8, 20, and 48 h. after administration. Histol. effects are described of N-acetyliodocochinol Me ether (Compound 368), a quaternary ammonium salt (Compound 707), α-phenyl-β-(3,5-diiodo-4-hydroxyphenyl)propionic acid (Compound 497), and podophyllin (Agent 85V); all injured the tumor cells. Podophyllin interfered with mitosis in sarcoma, epidermis, and intestine cells of mice, produced necrosis in Rous sarcoma of chickens, and damaged cerebellar Purkinje cells in chickens.

IT **65967-01-3**, Dibenzo[a,c][1,3]cycloheptadiene, 7-acetamido-1,2,3,9-tetramethoxy- **640735-77-9**, Colchinol, N-acetyliodo-, methyl ether
(necrosis by)
RN 65967-01-3 CAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-3,9,10,11-tetramethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 640735-77-9 CAPLUS
CN Colchinol, N-acetyliodo-, methyl ether (5CI) (CA INDEX NAME)

Absolute stereochemistry.